CARDIAC THERAPY

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Preface

When it was suggested that I write a book on the treatment of heart diseases I welcomed the opportunity of crystallizing my experience in a more formal way than is possible in papers or in clinics and lectures Although some of my friends who had written books told me of the continual revision which text books require and warned me of the moderate slavery to which it committed the author, I acquiesced It was only after many months of preparation that I came to realize what I had undertaken.

Definition of the scope of a book on treatment offers many difficulties. Since the principal intent is the presentation of therapy, knowledge on the part of the reader concerning etiology, pathology, and natural history of the various diseases must be in large part assumed. It must be emphasized however, that the management of disease, as distinguished from the mere application of specific remedies, implies an exact understanding of functional pathology and in many instances of anatomy and pharmacology. It has been necessary therefore, to include in most chapters such data in an introduction which is selective rather than exhaustive and which varies in length with the requirements of each subject

In the discussions which follow it may appear to the experienced physician and cardiologist that I have devoted too much space to details. In many text books treatment is discussed in a general way which leaves the student and physician with the necessity of organizing the step-by-step management of the case which confronts him I have tried deliberately to present definite plans with indication of what regimens are employed, and what medications are used and in what amounts. While variations to meet specific indications are given appropriate space, the final adaptation which is the essential of good medical management has of necessity been left to the resourcefulness and intelligence of the reader

There is intentional duplication of material in several chapters. If the reader wants to know how to treat a disease he does not wish to lose continuity and become distracted by reference from chapter to chapter. A better rounded picture of the treatment of disease under consideration is achieved by arrangement of each part so that it can be read independently of other portions of

the book. However, this has not been possible in all instances as in the case of the use of digitalis, the symptoms and treatment of heart failure and cardiac irregularities, and other features which appear again and again in the symptomatology and management of cardiac difficulties.

The order of the chapters may require explanation. When a scheme was set up for arrangement of the chapters according to a rigid system there were obviously many chapters relating to special topics which did not fit into such a classification. For instance it was apparent that a vertical classification only, such as an etiologic basis, was not elastic or inclusive enough. Accordingly I have also made use of horizontal chapters. For example congestive heart failure, which may occur in all etiologic types of heart diseases, and important drugs such as digitalis and mercurial diuretics have been singled out for special consideration. The chapter relating to congestive heart failure has been placed first because it is common to so many forms of heart disease and is one of the most frequent sequelae of heart disease requiring therapy. The use of digitalis and of mercurial diuretics has been described briefly in this chapter to maintain continuity in the treatment of this state. It seemed, however, that more complete and fuller discussions of these two important drugs could best be provided in separate chapters in order to avoid interruption of the flow of this chapter. Then it appeared appropriate to place the chapter relating to anticoagulant agents, another group of drugs, immediately following. Irregularities of the heart required special treatment since they occur in so many forms of heart disease, and their early presentation appeared advantageous. Succeeding chapters take up treatment of various types of heart disease classified according to etiology. Brief discussions of diseases which may have cardiac manifestations or may simulate cardiac disease are grouped in one chapter. Then follow chapters on acute myocarditis, acute pericarditis, chronic constrictive pericarditis, and subacute bacterial endocarditis. The remaining chapters are devoted to special topics or special problems in the treatment of heart diseases: heart disease in the aged, heart disease in pregnancy, cardiac management of surgical patients, surgery in patients with cardiac disease, to mention a few. It is hoped that the chapter on diets will be of practical service in planning diets for cardiac patients not only when they are in bed at the hospital or at home, but also in their ambulant management.

While the function of a book such as this is primarily to relate well-established procedures and methods of treatment, I have tried to bring into focus new forms of treatment and new drugs. The surgical procedures used in the treatment of patent ductus arteriosus, of the tetralogy of Fallot, and for the correction of the defect in coarctation of the aorta have been performed on sufficiently large numbers of patients to have become accepted. Valvulotomy, commissurotomy, and manual dilatation in the treatment of mitral and of pulmonary stenosis are in the early stages of their development. Final evaluation

and indications for their use await application to larger numbers of carefully selected patients. Discussions of these new procedures have been included. New drugs which have already found a definite place in our therapeutic armamentarium have been given appropriate space. For instance the use of thiomerin, a new mercurial diuretic, has been fully discussed.

Now that supplies of the substance have become generally available, it seemed in order to mention the use of adrenocorticotrophic hormone (ACTH) in the treatment of acute rheumatic fever even though its ultimate place in this area of therapy cannot be predicted at present. Pronestyl (procaine amide) has been mentioned because it gives promise of being a useful drug in the treatment of ventricular and nodal paroxysmal tachycardias, although its introduction is so new that it has not had extensive trial. Since the treatment of cardiovascular syphilis with penicillin has in most clinics replaced the use of arsenicals and bismuth, only the use of the former has been described. Those interested may find discussions of the latter by reference to earlier textbooks.

In calling attention to each new drug or form of therapy an appraisal of its present status has been attempted, based on our own clinical experience at the New York Hospital as well as a survey of the latest reports from other clinics.

In some parts of the book I have used illustrations to demonstrate the effects of treatment. The added clarity achieved by use of such illustrative material is particularly evident in presentations of irregularities, and of the effects of digitalis and of diuretics.

I have paid much attention to the relation of surgery as well as other specialties to the treatment of heart diseases. Unless the physician has observed many operations and has watched the behavior of cardiac patients during the stress of surgical manipulation and anesthesia, he cannot correctly advise his patients concerning appropriate treatment. In many instances the care of the patient should be a joint cooperative effort preceding, during, and after surgical intervention This is true of all surgical procedures, but is especially pertinent to cardiac surgery. If I have written at some length of the treatment of chronic constrictive pericarditis, it has been with the intent of illustrating the point and of demonstrating how the physician, by being part of the undertaking, may contribute to the benefit of the patient.

Medical management is more than the administration of drugs or arrangement for specific measures. I have tried to communicate what it means when you tell a patient that you will take care of him when he asks you to be his physician. He must be comforted, he must be inspired with confidence that you can help him. He must be treated as a person and not as a disease. This point of view is important and has been elaborated particularly in the chapters relating to rheumatic fever, hypertension, angina, and myocardial infarc-

tion. The interest of the physician must extend beyond the patient to his family and friends. Those of us who have had the psychosomatic aspects of treatment in mind are pleased at the interest which is now accorded this phase of medicine, and I have tried to weave into the account some indications of how they may be approached.

In a sense, the book has been written dogmatically since throughout I have wished to reflect my own notions of treatment. When there are opposing points of view, however, I have described them and have given the reason for the plan which I have preferred. When new procedures have not been fully tested they have been described with reservations.

I cannot leave this foreword without a word of acknowledgment to my early teachers. First, my association with Dr. Edward Perkins Carter at the Heart Station at Johns Hopkins Hospital stimulated my interest in cardiovascular diseases and the study of the circulation. Following this came my long years of association with Dr. Alfred E. Cohn at the Hospital of the Rockefeller Institute for Medical Research. In addition to being an able scientist and investigator he is a wise physician who made an indelible impression on my thinking, which will no doubt be seen in many places in this book. I owe much to the wise guidance but complete freedom of work under Dr. Eugene F. DuBois and Dr. David P. Barr at the New York Hospital-Cornell University Medical College. My gratitude also goes to the long line of resident physicians with whom I have had the privilege of studying: to Deitrick, Wheeler, Crane, Smith, Seal, Horger, Shepard, Bennett, Pritchett, Weiman, Thompson, Bailey, Kirk, McCoy, Sorenson, Luckey, and Watson to name only a few who remained long, worked faithfully, and influenced my thought and development.

I am indebted to my many colleagues who have read the chapters and provided helpful criticisms I am very grateful to Miss Betty Richmond of the Department of Nutrition for her help in preparation of the chapter relating to diets. And finally I wish to thank the publishers for their interest in the manuscript and for their helpful suggestions during its preparation.

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CARDIAC THERAPY

CHAPTER 1

Congestive Heart Failure

Congestive heart failure is said to be present when the heart is unable to meet demands which are placed upon it. Dyspnea and orthopnea, venous engorgement, râles in the lungs, pleural effusion, ascites, enlargement of the liver, edema, and appearance of or change in degree of cyanosis are the most prominent and most common manifestations and may appear in various combinations and degrees. Congestive heart failure is also known as cardiac decompensation, cardiac insufficiency, heart failure, and cardiac incompetency.

The manifestations of heart failure of the congestive type are essentially the same regardless of the etiology or of the anatomic defects which may be present Sometimes peripheral edema predominates; at other times pulmonary or abdominal manifestations prevail The terms "forward" and "backward" failure are neither useful nor accurate and should be discarded "Forward" failure is said to be due to low cardiac output, and "backward" failure to increased peripheral and pulmonary venous pressures Back pressure can occur only if the blood fails to go forward, failure of the blood to go forward must result in back pressure provided the volume of circulating blood does not decrease. According to the "forward" failure notion *salt and water are first retained in the tissues, due to impaired renal excretion, thus* increasing the extracellular interstitial fluid. Venous pressure rises later. According to the "backward" failure hypothesis, the venous pressure rises first and is the primary cause of edema

On the other hand, the patterns of clinical heart failure do not fall into such sharply defined categories as left-sided and right-sided. The critical analyses by Luisada and Starr of these concepts point up the lack of basis for the classification. At the time these patients are seen they usually exhibit in varying degrees most or many of the features which make up the picture of clinical heart failure, and it is not possible to separate right and left components

Richards, after extensive studies of the circulation in congestive heart failure with

the technic of right heart catheterization, believes that the phenomenon of congestive heart failure is essentially a disturbance in pressure values rather than in flow of blood. In the "right-sided" failure pressures in the right auricle and peripheral veins are essentially *the same*; *"left-sided" congestive failure produces greatly* elevated pressures in the lesser (pulmonary) circuit and in the right ventricle Hypertensive congestion in the lesser circuit is the dominant factor in the latter type.

There is evidence that the cardiac output is low in the most common types of congestive heart failure: the hypertensive, the arteriosclerotic, the rheumatic, and the syphilitic. This was the case in patients studied by the Grollman technic (Stewart) (Figs. 16 and 17) and confirmed by the newer technics of cardiac catheterization (Hickam and Cargill) (McMichael) (Richards and Cournand) (Stead) There are, however, certain occasions when the heart fails with a normal or even with an increased cardiac output, hyperthyroidism, arteriovenous communications, Paget's disease, anemia, pulmonary heart disease, and beriberi heart disease serve as examples. A statement about heart failure and cardiac output which would probably apply to all of these situations is that the cardiac output is low in relation to the metabolic needs of the body.

Starling's law of the heart finds application in congestive heart failure. This law, formulated from observations on heart-lung preparations, states that *the cardiac output increases with successive increases in diastolic volume of the heart, up to a certain point. Beyond this, further stretching of the heart results in decrease in* cardiac output (p. 69). Richards suggests that instead of relating cardiac output to diastolic heart volume, a more useful relationship would correlate cardiac output and diastolic filling pressure

In most instances of clinical heart failure, with the exceptions which have been cited, the cardiac output per minute and per beat are decreased, the circulation time is prolonged, the venous pressure is elevated, and the blood volume is increased. Recent observations of Ross and others using radioactive phosphorus-tagged red blood cells indicate that the circulating blood volume is not increased in congestive heart failure. The basal metabolic rate may be elevated during heart failure and fall with return to compensation (Stewart) *With the restoration of compensation all* of these measurements again approach normal levels

Predisposing Causes

Congestive heart failure occurs in the following forms of heart disease:

1 rheumatic heart disease, in the stage of either acute carditis or chronic valvular disease;

2. arteriosclerotic heart disease;

3 coronary artery disease with and without myocardial infarction,

4. myocardial fibrosis;

5. heart disease due to hypertension;

6. syphilitic heart disease in which there may be aortic insufficiency, aneurysm, coronary artery involvement, and occasionally myocarditis;

7. congenital heart disease;

8 so-called pulmonary heart disease, in which a lesion within the lungs places a burden on the heart (emphysema, chronic bronchitis, pulmonary fibrosis, pul-

monary arteriosclerosis, or Ayerza's disease may be causes of increase in pulmonary arterial pressure);

9. chest deformities such as kyphoscoliosis,

10. Graves' disease, either from persistent sinus tachycardia and the large oxygen requirements or because of the onset of cardiac irregularities.

In addition a patient with any type of organic heart disease may be in a good state of compensation until congestive heart failure is precipitated by the onset of a cardiac irregularity, or by an acute infection, pregnancy, acute exertions, stress of surgical experiences, postoperative overloading with fluids, the strain of some intercurrent illness, or myocarditis. Heart failure may occur when amyloid disease involves the heart. It has been recorded in hemochromatosis.

Functional Capacity

Patients with chronic heart disease usually suffer a gradual decline in the functional capacity of the heart. Fatigue and dyspnea appear early and increase gradually. Later the other signs and symptoms of heart failure may be added. The progress of symptoms may be so gradual—the patient becoming accustomed to each new increment of disability—that the fully developed picture of congestive heart failure may be present by the time the condition has become severe enough for the patient to see a physician. At other times the onset of signs and symptoms is rapid and leads the patient to seek treatment early, perhaps immediately. At still other times the onset of failure is even more rapid—a matter of minutes or hours—not only in patients with preexisting organic heart disease, but also in those with acute damage to the heart, such as myocardial infarction and acute myocarditis.

The physician may see the patient within a short time of the onset of heart failure when there may be dyspnea alone or moderate edema. Other patients may be seen after the onset of failure resulting from the stress of an acute respiratory infection, and still others in a state of chronic congestive failure of months' or years' duration after having received varying forms of treatment over this period. Patients may be seen with successive bouts of heart failure, they may enjoy freedom from signs and symptoms of decompensation in the intervals between attacks if proper therapy is maintained. Finally, some patients are seen in acute pulmonary edema or during attacks of nocturnal dyspnea.

MANAGEMENT OF THE PATIENT

Objectives in Treatment

The objectives in the treatment of congestive heart failure are twofold: (1) to restore the patient to a state of compensation, so that there is freedom from the signs and symptoms of heart failure; (2) compensation achieved, to return the patient to as much activity as is compatible with the functional capacity of the heart, without the recurrence of heart failure, on whatever medications are required. Frequently there has to be a compromise in these objectives.

If the patient is not too sick he should be told in simple terms about his illness, how heart disease has resulted in heart failure, and the objectives of treatment. In this way cooperation can be obtained and the patient is made aware of the reasons

for using the measures which are employed. If the patient is too sick to follow this orientation, his illness is discussed with him as soon as his condition permits.

The regimen usually employed in the treatment of congestive heart failure is made up of some or all of the following measures: bed rest, low salt diet, low fluid intake, digitalis, one of the mercurial diuretics, ammonium chloride, oxygen, and sedatives.

Bed Rest

It is my practice to keep patients at rest in bed until they are free of signs and symptoms of congestive heart failure, namely, until the heart rate has been slowed,

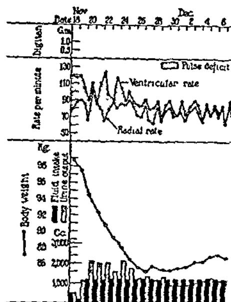


Fig 1.

Effects of Rest in Bed and Restriction of Fluid Intake on Urine Output and Weight of Patient Suffering from Congestive Heart Failure. Auricular fibrillation was present On these measures alone without medication there was immediate diuresis and a loss of 14 Kg of weight in ten days Ventricular rate fell and pulse deficit decreased (Stewart, H. J · Mechanism of diuresis Alterations in the specific gravity of the blood plasma with onset of diuresis in heart failure *J. Clin Investigation* 20 1, 1941)

venous engorgement has disappeared, dyspnea and orthopnea have lessened or disappeared, pleural effusion has been absorbed, râles are no longer heard at the lung bases, ascites and edema have cleared entirely, and the liver has disappeared under the costal margin or become smaller, has reached a stationary size, and is no longer tender. It may require days, weeks, or months to achieve this optimal state.

The degree of rest indicated varies with the severity of the heart failure. For example, early failure with pitting edema at night can be managed without complete bed rest, perhaps even on an ambulatory basis. But for patients with the full picture of cardiac decompensation rest *in bed is indispensable*, especially when much discomfort and dyspnea are present, and if it should be the first attack of

heart failure Prompt and vigorous therapy for a first attack argues for quick restitution of compensation, and prevents progression to more serious stages and permanent and further restriction of the functional capacity of the heart. Patients who have had repeated episodes of failure or who have chronic congestive heart failure can frequently be restored to a more satisfactory state or to compensation by modification of the full bed rest program or even by an ambulatory regimen, although these may not be the optimal plans of therapy.

A period of rest in bed attains two *objectives*: (1) Compensation is more readily restored. (2) It defines the best state of compensation the patient can attain at rest. Besides, diuresis with loss in weight may result from rest in bed and restriction of fluid intake without the use of diuretics (Fig. 1).

Complete rest in bed means that a bed bath is given and a bedpan is used for bowel movements. For patients with moderate failure and for aged patients this strict schedule is modified. Because of renal involvement, nitrogen retention, and the risk of thrombophlebitis and of bronchopneumonia, it may be unwise to immobilize the latter completely. I may allow these two groups of patients to sit in a chair at the bedside for a part of the day, and to use a commode.

Bed patients may be propped up by pillows, by a backrest, or by a Gatch bed, in whatever position they find most comfortable. They are encouraged to move their legs to prevent stasis, and are instructed not to lie with their legs crossed, since this will obstruct the venous return They are instructed to breathe deeply six or eight times every one to two hours; this expands the lungs and prevents stasis. With these attentions to the peripheral circulation and to the lungs, thrombophlebitis and pulmonary infarction occur less frequently.

Bed rest is instituted in order to relieve the heart of as much work as possible, although it is obvious that the heart cannot be put at complete rest. The basal condition is the best that can be attained in requiring a minimal amount of work of the organ; anything short of the basal state puts an additional burden on the heart. Hickham and Cargill have shown that patients with congestive heart failure can attain little or no increase in their basal cardiac output during exercise, but only an increase in their arteriovenous oxygen difference. It appears that the resting cardiac output in congestive heart failure is the greatest that can be managed except transiently, and even at rest it may not be commensurate with the metabolic needs of the tissues. Requirements for extra flow to working muscles, for instance, can be met only by diverting blood to these areas from regions in which essential metabolic processes are going on. A deficit is incurred which must be repaid.

Thus there is adequate reason for the use of rest for these patients Moreover, I have not seen harm from putting patients with heart failure to bed It is rare that episodes of embolic phenomena in these patients can be attributed directly to this practice Neither have I been impressed with the increase in dyspnea with the shifting of fluids from the extremities to other locations in the body The observations of Deitrick and his associates on the effects of immobilization and bed rest are not applicable to these patients, as they are not completely immobilized. The wasting which accompanies complete immobilization is not encountered in patients who move freely in bed The muscles of the calves may become flabby but this is quickly remedied when the patient begins sitting up I have not observed renal

calculi whose formation could be attributed to bed rest in patients with heart failure and coronary thrombosis

The very sick patient should not feed himself. With improvement, though, he may be allowed to feed himself first one meal a day, then two, and finally all three meals If the patient is not very sick and not unduly weak, feeding by a nurse or attendant is not necessary.

Sleep

The patient should have adequate sleep It is best to be certain that he rests at night so that he may be awake during the day, except for a rest period after lunch. Pentobarbital sodium 0 1 Gm may be given at bedtime and repeated in three to four hours if necessary Phenobarbital in 30- to 60-mg. amounts may be used. Whisky 30 to 40 cc. at bedtime may increase the effectiveness of these drugs. For certain patients paraldehyde by mouth, rectum, or intramuscularly in 8- to 16-cc. amounts may be useful and for others triple bromides or chloral hydrate may be adequate (see Sedatives, p. 19).

Care of the Bowels

There should be a daily soft bowel movement. If the patient is very sick and receiving a great number of medications it may be necessary to resort to enemas instead of cathartics. Mild cathartics should be used at once when morphine and codeine are being given in order to prevent constipation and the possibility of fecal impaction Milk of magnesia 30 cc. at night may be sufficient. On the other hand cascara sagrada or compound licorice powder together with small amounts of milk of magnesia and mineral oil will be effective.

Diet

The diet should be a balanced one within the restrictions which may be necessary. Principles to be observed are limitation of salt intake with as much protein as the restrictions permit, together with adequate quantities of fresh vegetables and fresh fruits, and supplementary vitamins as required. A soft diet, or in some cases a full liquid diet, may be required for a few days for patients who are very sick, if the appetite is failing, or if there is nausea and vomiting Such a diet would include salt-free cereals, soft and poached eggs without salt, salt-free bread toasted, milk toast, custards, junket, and similar foods Daily food allowances and sample menus are given in Chapter 34

If dehydration and acidosis are to be prevented, *careful nursing supervision* is necessary to be certain that patients eat adequately and take the allotted amount of fluid. If vomiting persists it may be necessary to give 5 per cent glucose by hypodermoclysis or intravenously even though the patient is suffering from heart failure.

Sodium Restriction

In many instances, patients on the usual medical regimen of restricted fluid intake, digitalis, and mercurial diuretics may regain compensation on diets containing 3.0 to 5.0 Gm. of sodium chloride daily, or even on an unmeasured diet to which no extra salt is added. However, for the average patient the total intake of

sodium chloride in 24 hours should be limited to 2.0 Gm. or less. This will necessitate the use of salt-free butter and bread and vegetables with a low salt content, and in most cases will be unobtainable if a glass of milk (200 cc.) is included in the diet. Salt-free canned foods are too expensive for general use and are not necessary.

In treating certain patients suffering from congestive heart failure even more rigid restriction of the salt intake—to 0.5–1.0 Gm. a day—must be enforced for the *mobilization of fluids. It is difficult to supply an adequate protein intake with this* salt restriction so that a salt-free dried milk such as Lonalac and careful selection of the foods are even more necessary These schedules are supplied in Chapter 34.

The salt in the diet is restricted because the sodium ion increases the retention of water. Observations made by Burch and his associates with the use of radiosodium, Na^{24} and Na^{22}, show retention of sodium during heart failure. Retention is most marked as heart failure is appearing or as it is getting worse. With diuresis and restoration of compensation the excretion of sodium is increased. It has been found that when radiosodium is given to normal subjects approximately half of the total sodium of the body is excreted in 15 days. On the other hand, about 40 days elapse before patients with congestive heart failure excrete this amount. Mercurial diuretics increase the excretion of sodium to normal levels in patients with heart failure Giving sodium to patients with heart failure does not result in greater excretion of this ion but in its retention.

Care must be exercised to be certain that patients on low salt diets are not given sodium salts in medications For example, they should not be given sodium bicarbonate nor saline cathartics such as sodium phosphate.

When sulfonamide drugs must be given sodium bicarbonate may not be necessary. When the salt is absolutely required caution and constant supervision are required in order to detect adverse changes in the state of compensation

Potassium bicarbonate should not be used as a substitute for the sodium salt. According to Stewart, Shepard, and Horger, the heart muscle may be poisoned by the potassium ion and auricular standstill may result (Fig 64) The lowered renal function with elevation in the blood urea nitrogen may decrease the excretion of potassium until its blood level rises to a point which is toxic for cardiac muscle. *It is obvious also that potassium chloride should not be prescribed* as a diuretic in the treatment of congestive heart failure; I have seen auricular standstill and death result from it (Fig 21) There is further discussion of dangers from the use of potassium in Chapter 31

The low salt diet can usually be managed in a hospital. Still it is wise for the physician to see the patient at mealtime occasionally and observe the accuracy with which the orders are being followed. The patient is warned *not to use salt* even though the salt container should be placed on the tray by error, and not to eat butter should it taste salty. These precautions may obviate weeks during which no headway is made in reduction of fluid accumulations because of laxity in following recommendations. If the patient is at home directions must be given about the preparation of food Under such circumstances work in the preparation of the special food may be reduced by cooking vegetables and meat for the whole family

without salt, then setting aside the patient's portions and seasoning the remainder for the family.

The "rice diet" should not be used as an easy way to provide a salt-poor diet for patients with congestive heart failure. Patients on this diet should be kept under close supervision. Other measures, such as diuretics, which are required in the treatment of heart failure may make these patients more susceptible to the deleterious effects of the rice diet—namely sodium depletion.

SALT SUBSTITUTES. Salt substitutes are apt to be abused, even though their medicinal role is stressed, and they should not be prescribed for patients on a low salt diet. Potassium chloride and lithium chloride, which are the most common ingredients of these imitations, may be harmful for certain patients even in moderate amounts. Patients may use enough after some days for toxicity to result.

Lithium chloride has caused the more serious toxic effects. The toxic agent is the lithium ion. The symptoms are drowsiness, weakness, and generalized tremors. Mental changes, staggering gait, reflex hyperactivity, and coma with death may follow with continued use. The toxic effects of lithium chloride are enhanced by prolonged periods on low salt diets and by impairment in renal function One of the fatalities which has been reported from its use occurred in a patient who was on a rice diet. My attention was directed to the toxic effects of lithium chloride as a salt substitute by the history of a patient who suffered weakness and generalized tremors. Such amounts were used on all foods that even a dinner guest had the toxic symptoms of nausea and diarrhea on two occasions a week apart This occurrence led to the detection of the salt substitute as being responsible for the patient's symptoms After the patient stopped using this substance her symptoms disappeared promptly. Lithium poisoning should be treated by the intravenous administration of saline with glucose.

SALT DEPLETION. With the renewed interest in the role of sodium in edema and the marked restriction of sodium in the diet, together with too frequent use of mercurial diuretics, instances of harm resulting from sodium depletion are coming to light. Peters has directed attention to the possibility, after prolonged periods on a limited salt regimen, that diuretics may fail to be effective because sodium is not available to carry off water in the urine. There has been a recent report of uremia due to sodium depletion. This occurred during the treatment of congestive heart failure in a patient with hypertension who was subjected to diuresis by mercurial drugs. The blood urea nitrogen should be measured in patients who are subjected to prolonged diuresis especially when there is evidence of impaired renal function. *Salt should be restored to the diet if a rise in blood urea nitrogen occurs.* Peters has recommended the use of hypertonic salt solution to restore sodium chloride when there is evidence of salt depletion.

Protein Requirements

In view of the low level of the serum proteins in some patients with congestive heart failure, it would be advantageous to have adequate amounts of protein in the diet. Because of the high salt content of meat this constituent of the diet is difficult to manage if the total salt content is to be kept within the 2.0-Gm. limit.

Lonalac, because it is salt free, may be useful in supplying a part of the protein. Freshwater fish should be used rather than the salt water varieties.

Vitamins

Vitamin supplements may be required to maintain an adequate diet. Because of the restrictions which are necessary to keep the salt content of the diet low, these constituents may be inadequate over long periods of time. Vitamin B maintenance is especially important because this complex may be compromised by the restriction in the amount of meat. Even on a fluid intake of 1200 cc. in 24 hours, 200 cc. of citrus fruit juice can be provided daily.

Fluid Intake

The fluid intake in 24 hours for most patients with congestive heart failure should be restricted to 1200 cc.; for a few, limitation to 1500 cc. may be adequate. Amounts greater than these should not be permitted without compelling reasons. A fluid intake of 1200 cc. in 24 hours provides approximately six ordinary size

namely milk—within the salt limitation—coffee, beverages, and soup. Soups should usually be avoided because they do not allay thirst and their water content is usually too high in proportion to the food value. Watery fruits should be avoided, unless their water content is calculated. I have frequently seen patients fail to exhibit appropriate diuresis and loss of weight on a particular regimen, to discover that they were eating oranges, plums, grapes, melons, and other fruits, all having high water contents. When these fruits were discontinued, improvement ensued. When patients suffer from infections associated with fever, it may be necessary to increase the fluid intake to 1800 cc. or more per day. With the low salt diet patients manage on the low fluid intake even in hot weather. Diuresis may result from restriction of fluid intake and rest in bed before diuretics are given (Fig. 1).

The restriction of the fluid intake in the management of congestive heart failure has been discarded by some physicians. In my experience, even though the salt limitation is rigid, restriction of the fluid intake is also necessary with most patients suffering from heart failure, if they are to be made free from accumulations of fluid. Several recent papers have advocated that fluids be forced, or that they be allowed ad libitum, or that 2000 to 3000 cc. of fluid be given daily in the treatment of congestive heart failure. However, the charts which accompany these reports have not

tive. When these symptoms persist and the patient shows evidence of acidosis, such as an acetone odor to the breath and acid bodies in the urine, it may be necessary to give 5 per cent glucose by hypodermoclysis. One to one and one-half liters may be given in 24 hours. If edema is so marked that absorption of the fluid by hypodermoclysis cannot be accomplished promptly, it may be necessary to give 5 per cent glucose slowly by the intravenous route. Careful observation should be

made during the infusion to detect increased distention of the veins and pulmonary stasis. These measures are rarely necessary unless there are complications such as surgical operation, cerebral accidents, and diabetic acidosis.

When extreme restriction of the salt intake to 0.5 Gm. is required it may be necessary to have the patient drink distilled water rather than tap water, inasmuch as the salt content of the water in different cities varies greatly

Schemm Regimen

The principles of this regimen are: (1) a low salt diet yielding an acid ash residue, and (2) the requirement that the fluid intake be forced to 5000, 6000, or 7000 cc. a day. Dilute hydrochloric acid is added to the water and ammonium chloride is also used to insure the excretion of an acid urine. Schemm reported excellent diuresis from this regimen in the treatment of congestive heart failure. However, on analysis of the charts which were reproduced, it was seen that the volume of urine rarely exceeded the fluid intake except on the days when mercurial diuretics were given We (Newman and Stewart) were unable to free patients of congestive heart failure on this regimen carried out exactly as Schemm recommended. Consequently we do not recommend its use. Nevertheless a brief description of the diet schedule is given in Chapter 34, for those who wish to try it.

Karell Diet

There has been a tendency among some physicians to revive the Karell diet in the last few years. The total food and fluid intake in 24 hours is limited to 800 cc of milk. No other food or fluid is allowed. The milk is given in 200 cc. amounts four times a day. I used this diet some years ago but have had rare occasion to do so in recent years. If it is adopted, it should be used for a few days only. It is deficient in calories, in protein, in iron, and in vitamins. Its usefulness depends on its low salt content—approximately 1.0 Gm.—its low total fluid content, and its low food value. These objectives can be attained with more palatable and more varied foods if a diet which is low in salt is prescribed together with the restriction of the fluid intake to 1000 cc. or 1200 cc. Nothing is gained by this regimen that is not attained in a more palatable way by the use of a more liberal diet. When the patient is at home and there are difficulties in providing a salt-poor diet and in managing the low fluid intake, the Karell diet may find a short period of usefulness, but it must be recognized as an emergency measure. The provision of a more liberal diet prepared without salt must ultimately be made.

DRUGS USED IN TREATMENT OF CONGESTIVE MANIFESTATIONS

Diuretics

Certain drugs are used in the treatment of congestive heart failure because they induce diuresis. They mobilize fluid accumulations which are the mainfestations of congestive heart failure, causing the fluid to be excreted as urine. Consequently the symptoms may be alleviated and the signs of failure may diminish or disappear.

Digitalis

Although a brief outline of the use of digitalis will be given at this point, Chapter 3 should be read to gain insight into what the drug can accomplish and the mechanism of the action of the drug in congestive heart failure.

The cardinal indication for digitalis is congestive heart failure. Contraindications to its use in this situation are indeed few. Digitalis should be used promptly and in adequate therapeutic amounts The preparation which is to be used and the route of administration in any particular patient depend upon the severity of the heart failure and the rapidity with which an optimal effect is desired. Digitalis is effective not only in patients with auricular fibrillation (Fig 13) but also in those with normal sinus rhythm (Fig. 14). It may induce satisfactory and adequate diuresis so that other diuretics may not be required (Figs. 13 and 14). In this connection it should be emphasized that mercurial diuretics do not take the place of digitalis in the treatment of heart failure, but rather are used to induce further diuresis when it is required.

The method of standardization and determination of the dosage are described in Chapter 3. The amount which, if given over a 24-hour stretch, or at one time, is adequate to slow the ventricular rate in auricular fibrillation with a rapid ventricular rate to around 70 to 75 beats per minute is called the *digitalizing amount*. This is also the optimal therapeutic amount in patients with congestive heart failure. These data can be transferred to patients with normal sinus rhythm, in whom the heart rate does not serve as a guide to digitalization. The *maintenance amount* is that dosage which, given daily, will keep the resting ventricular rate at the same level of 70 to 75 per minute. In patients with auricular fibrillation the plan would be to give the digitalizing amount within 24 hours or less, but again the slowing of the ventricular rate would serve as a guide. In patients with normal rhythm the plan would be to give the full digitalizing amount unless toxic effects occurred.

Digitalization should be accomplished in most instances without the induction of nausea and vomiting and other toxic effects. One should be certain about the patient's use of digitalis within the previous two to three weeks, especially if the drug is now to be used intravenously.

WHOLE DIGITALIS LEAF. For most patients with heart failure the administration of the whole leaf (U.S P XIV) is satisfactory for digitalization and ration doses Maintenance is more easily managed without toxic effects over a long period of time than with digitoxin.

The average *digitalizing amount* of the whole leaf (U.S P XIV) is 1 8 Gm if given within 24 hours This is given in broken doses as follows: 0 8 Gm. followed by 0.5 Gm. in four to five hours, 0 3 Gm four to five hours later, and 0 2 Gm after another four to five hours. If auricular fibrillation is present the ventricular rate serves as a guide. Slightly more or slightly less than 1 8 Gm. may be required for certain patients With the ventricular rate slowed, the average *maintenance dose* of 0.2 Gm. daily may be required, but this is adjusted to keep the resting ventricular rate around 70 per minute. The adjusted dose may be 0 1 Gm. alternating with 0.2 Gm. or 0.1 Gm daily, or rarely 0 3 Gm. or more. The digitalizing amount is approximately the same for all patients, but the maintenance

dose varies with the rate of excretion. With digitalization the ventricular rate slows, dyspnea becomes less marked, diuresis occurs, and the patient improves (Fig. 13).

When normal rhythm is present, the same amount, 1.8 Gm., is given in 24 hours, according to the same schedule. The drug is discontinued if toxic effects appear, but these occur rarely on this amount. The average maintenance amount, 0.2 Gm., is then given daily, although over a long period this may prove to be too much and the dosage may be reduced. With progress of digitalization in this group of patients with normal rhythm, dyspnea diminishes, diuresis occurs, and the patient improves (Fig. 14). The heart rate may become slower.

If the patient has already had digitalis the amounts given in order to complete digitalization are adapted to the estimated stage of digitalization. If digitalis has already been standardized and the patient has not had digitalis within two to three weeks the total digitalizing amount may be given at once, although this course is usually not followed. Two to three weeks are required for the complete excretion of digitalis leaf after digitalization has been attained.

DIGITOXIN—ORAL. As I have said, the whole leaf is satisfactory for the routine digitalization and maintenance of patients requiring digitalis, and is the preparation which I use under most circumstances Digitalization with digitoxin is more apt to cause nausea and vomiting than when it is attained with the whole leaf. However, the known and constant potency of digitoxin may occasionally be an advantage (p. 72). If digitoxin is used orally schedules similar to those which have been outlined for the whole leaf can be used, except that milligrams are substituted for grams. The digitalizing amount is 1.8 mg. in 24 hours, divided as follows: 0.8 mg., followed by 0.5 mg.; then 0.3 mg, and finally 0.2 mg. at four- to five-hour intervals. This schedule is used for patients with auricular fibrillation as well as for those with normal rhythm. The same precautions are taken with respect to toxic symptoms as when the whole leaf is used. A dose of 1.2 mg. which has been advocated is inadequate to digitalize most patients.

The average maintenance amount is 0.15 mg daily, with 0.1 mg. and 0.3 mg. as the extremes. Most patients require 0.1 mg alternating with 0.2 mg. Prolonged administration of 0 2 mg., which has been recommended as the maintenance amount, causes toxicity in many patients.

Maintenance over long periods is more difficult with digitoxin than with the whole leaf. Toxic effects during digitalization or during maintenance persist longer with this drug, as it is excreted more slowly.

Digitoxin by mouth is no faster in action than is the whole leaf.

DIGITOXIN—INTRAVENOUS. One of the advantages of digitoxin is that it is available for intravenous use. The same amounts are required to digitalize and to provide maintenance as by the oral route, namely, 1 8 mg., and it can be given on the schedules already stated Toxic effects have followed the use of as little as 1.2 mg. intravenously. Certainty about previous digitalization should be established before it is given. Since digitoxin for intravenous use is dissolved in 40 per cent alcohol, it should be diluted with normal salt solution.

Intravenous digitoxin is useful for patients who are nauseated and are vomiting and cannot take the whole leaf, and for surgical patients who are not permitted

oral medication. Since the same amounts are required orally and intravenously, a change from one route of administration to the other is readily accomplished.

Digitoxin orally and intravenously ordinarily achieves the same effects as the whole leaf: slowing of the ventricular rate in auricular fibrillation, diuresis, and restoration of compensation. There are, however, certain patients with auricular fibrillation in whom the ventricular rate is not adequately controlled even with large amounts of digitoxin, or in whom there are alternate bursts of rapid and slower rate. In many of these patients more satisfactory slowing of the ventricular rate can be achieved with the whole leaf. Another matter of concern in the use of digitoxin is the increase in the occurrence of auricular paroxysmal tachycardia with 2:1 heart block. For this reason I seldom use digitoxin intravenously.

The effects of digitoxin intravenously are not significantly more rapid than by the oral route (Tables I and II, pp. 74–79).

Two to three weeks are required for the excretion of digitoxin after digitalization —by either the oral or intravenous route.

AMBULATORY DIGITALIZATION. Digitalis leaf and digitoxin can be used for ambulatory digitalization. The digitalizing amount, plus the total maintenance amount over the number of days during which digitalization will take place, is spread over the number of days decided upon. Larger doses are given first and smaller ones toward the end of the digitalization period This is more fully described in Chapter 3, page 95, and a schedule is shown in Table III, p. 95.

Rapidly Acting Glycosides

When a rapid digitalis effect is required, as in severe heart failure and acute pulmonary edema, a rapidly acting glycoside should be used intravenously Ouabain and lanatoside C are suitable for this purpose. Digoxin is available for oral use.

OUABAIN. This glycoside—obtained from *Strophanthus gratus*—is used only intravenously, because it is not absorbed from the gastrointestinal tract. Slowing of the ventricular rate in rapid auricular fibrillation occurs within a matter of minutes (Table II pp. 78–79). If the patient has not had any digitalis, 0 5 mg. can be given at once, followed by 0.1 to 0 2 mg. amounts at one-half to one hour intervals until a total of 1 0 mg has been given Ouabain is excreted within 24 hours and is not suitable for maintenance.

LANATOSIDE C. This glycoside is obtained from *Digitalis lanata* leaf. Its effects when given intravenously are apparent almost as soon as those of ouabain. The intravenous digitalizing amount is 1.6 mg which may be given in one dose. It is excreted within 72 hours (Chapter 3, Tables I and II, pp. 74–79). The oral daily maintenance amount is 0 5 to 1 0 mg, the intravenous 0 2 to 0.4 mg. Intravenous lanatoside C is especially useful in the treatment of paroxysmal tachycardias. I prefer this drug to ouabain for rapid digitalization.

This drug is also satisfactory for initial oral digitalization and maintenance but the management may be more difficult than with digoxin, 7 5 mg. is the average amount.

DIGOXIN A glycoside derived from *Digitalis lanata* leaf, digoxin is useful for rapid oral digitalization and maintenance owing to its short latent period (almost as short as that of ouabain) and to its rapid rate of dissipation (Tables I and II,

pp. 74-79). If toxicity occurs it is of brief duration. Because of its rapid excretion, maintenance is not as easy as with the whole leaf. The average digitalizing amount is 3.75 mg., the range being 2 to 5 mg. It is excreted within 72 hours. The average maintenance dose is 0.75 mg. daily.

Digoxin is not very soluble in water; accordingly, it is not useful for rapid intravenous digitalization of patients with heart failure because of the volume of fluid

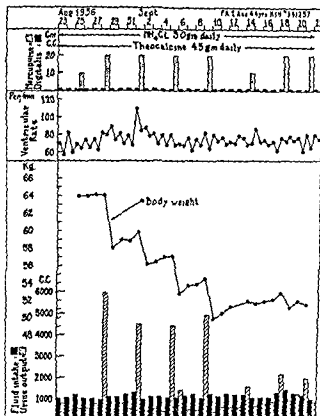


FIG 2.

Diuretic Effect of Mercupurin ("Mercuzanthin"), Given Intravenously in the Case of a Woman

14 526, 1937)

which must be introduced. However, its effect by this route is rapid—within the range of ouabain (Tables I and II, pp. 74-79).

Mercurial Diuretics

The mercurial diuretics are usually effective for the mobilization of fluid in congestive heart failure (Figs 2 and 3). However, they should be used as adjuncts to digitalis in the treatment of heart failure, not as replacements (see p. 37). Mercurial diuretics are discussed more fully in Chapter 2.

ROUTES OF ADMINISTRATION. Preparations are available for intravenous and intramuscular use (mercuzanthin, thiomerin, mercuhydrin, and salyrgan-theophylline), for subcutaneous use (thiomerin), for oral use (mercuzanthin and salyrgan-theophylline), and for rectal use (mercuzan). Until recently intravenous and intramuscular routes were most commonly employed, but with the introduction of thiomerin, a subcutaneous preparation became available which has found wide acceptance. I do not recommend the rectal or the oral route of administration. I use the intramuscular route less frequently than the subcutaneous and intravenous.

DOSAGE. The intravenous, intramuscular, and subcutaneous dosages are approximately the same, 1 to 2 cc. being most commonly employed I do not recommend the daily use of any of these preparations even in small amounts. It is much more satisfactory to give them every third day, two free days being allowed for restoration of the electrolyte balance and to avoid dehydration.

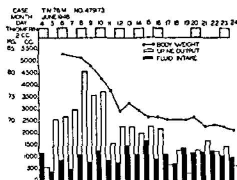


FIG 3

Diuretic E[illegible]
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Unless there is urgency, 1.0 cc. of the mercurial may be given first as a trial dose. It may be adequate and be used subsequently. For other patients 1.5 cc. is sufficient but 2.0 cc is most commonly employed. It is given at three-day intervals and not oftener than every second day. On the days when the drug is not given the weight *rises, though not to its former levels, and gradually the accumulated fluid is* eliminated. As the patient improves and compensation is restored it may be possible to increase the intervals between injections to as much as two weeks. It is better to maintain the patient on a regular regimen so that the weight varies within narrow limits only, than to have larger weight gains with marked fluid accumulations which require more vigorous therapy.

DRUG OF CHOICE Until recently the drug of choice in our clinic was mercuzanthin intravenously. It is given slowly and we have seen no untoward effects. Now, however, thiomerin is used most frequently and it is usually given subcutaneously. In patients with marked generalized edema which may interfere with absorption and in whom a rapid response is necessary, or in patients with acute heart failure,

it is administered intravenously. Diuresis begins more slowly after subcutaneous thiomerin than after its intravenous use, but it is more prolonged and, in some patients, is greater. It is well to be familiar with and to have available several mercurial diuretics, for not all patients react in the same way; the effect of one mercurial diuretic will decline, and another substituted in its place will provide excellent diuresis; and finally certain of these drugs may induce toxic effects in some patients (fever, skin rash, hypersensitivity) while others can be used with safety.

Ammonium Chloride

Ammonium chloride may be given orally in 1.0-Gm. amounts (as enteric-coated pills) three to four times a day, to augment the diuresis of the mercurial drug (Fig. 2). The benefit from ammonium chloride is due to its acidifying effects. Since it is best to give only the medications which are required, it is well to test the effect of the mercurial diuretic alone, if good diuresis results ammonium chloride is not necessary. I give the drug daily, not only on the day before and the day of the mercurial injection Patients should look at their stools to see whether the enteric-coated pills pass through the gastrointestinal tract unabsorbed. Because the control period in any one patient may not be comparable to the test period, it is very difficult to demonstrate that increased diuresis occurs from the use of this salt. The patient may not be in the same fluid and salt balance during the control period before ammonium chloride is used as he is in the period when it is given. A plain biscuit may be eaten after taking the tablets in order to allay gastric irritation.

In some instances ammonium chloride keeps the urine output near the fluid intake on the days when the mercurial drug is not given. Occasionally acidosis results from the continuous use of ammonium chloride when it fails to give diuresis. Ammonium chloride is also used as a diuretic even though mercurial diuretics are not given

Potassium chloride should not be used as a diuretic in the treatment of congestive heart failure since toxic effects on the heart may result (Fig. 21).

Xanthine Diuretics

Among this group of diuretics are theocin (or theophylline), diuretin (or theobromine sodium salicylate), thesodate (or theobromine sodium acetate), theocalcin (or theobromine calcium salicylate), and aminophyllin (or theophylline ethylenediamine). *The last two are most frequently employed.*

THEOCALCIN (THEOBROMINE CALCIUM SALICYLATE). This drug given orally in 1.0- to 1.5-Gm. amounts three times a day may result in excellent diuresis. Its use may be sufficiently effective to free the patient of heart failure. It may be used to maintain an adequate urine output on the days that the mercurial drug is not given. Nausea and vomiting due to gastric irritation are less likely to occur with this theobromine drug than with other xanthine diuretics Eating a biscuit after taking the tablets may prevent these symptoms.

AMINOPHYLLIN (THEOPHYLLINE ETHYLENEDIAMINE). The oral administration of aminophyllin occasionally induces sufficient diuresis. *In other instances it may be* used as an adjunct to the mercurial therapy. Eating a biscuit after taking the tablets

may prevent gastric irritation. It is given in 0.1- to 0.2-Gm. amounts three or four times daily as tolerated.

Aminophyllin may be given in the form of suppositories in 0.5-Gm. amounts one to three times daily, when nausea is present and when a slow, prolonged effect is desired. This form of therapy may find application in the prevention of nocturnal dyspnea.

Aminophyllin 0.24 to 0.48 Gm. may be given intravenously slowly when acute pulmonary edema and acute heart failure occur. However, its effect is transient, and its use by this route is not satisfactory in the treatment of chronic congestive heart failure.

The simultaneous intravenous injection of aminophyllin and the mercurial drug, in order to enhance and maintain the diuretic effect of the mercurial diuretic is discussed on page 43.

Urea

Urea as a 50 per cent solution in 30-cc. amounts orally three times a day is often a very useful diuretic for patients in whom fluid accumulations are resistant to mobilization. It may be effective in keeping the urine output near the fluid intake on the days when the mercurial drugs are not given. If the solution is kept in the icebox and is given very cold mixed with a small amount of grape juice, the bitter taste is made less disagreeable. Urea does not increase the urea nitrogen in the blood even in patients who already have an elevated blood urea nitrogen.

Resins

Recently the oral use of cationic exchange or sodium removing resins has been tested in the treatment of cardiac edema. The resins adsorb salts and are excreted in the feces. Sodium ions are removed by these agents so that they are not available for retention of water. The addition of an anion exchange resin to the cation resin increases the sodium-removing capacity of the resin. It is alleged that, for most patients, when resins are used the usual amount of salt may be allowed in the food and in fact must be maintained if salt depletion is to be avoided. In certain patients salt must be restricted if the resin is to be effective. The resins adsorb not only sodium but also potassium and calcium, and this may result in sodium and potassium depletion. Preparations now on clinical trial are carboxylic acid resins in the ammonium or in the hydrogen form. Some preparations also contain a potassium resin, the potassium being supplied in an attempt to prevent hypokalemia. The dosage of these resins has not yet been defined. When they are used care should be exercised that acidosis, sodium depletion, and hypo- or hyperkalemia do not occur. Sodium, potassium, chloride, blood urea nitrogen, and carbon dioxide levels in the blood should be estimated frequently. Their use is contraindicated in patients with moderate renal insufficiency.

I have had some experience with Carbo-Resin,* which is a mixture of ion exchange resins in the following proportions: Alkylene polyamine resin (anion exchange) 12 per cent; potassium salt of carboxylic acid resin (cation exchange) 29 per cent, carboxylic acid resin (cation exchange) 59 per cent. The usual dose

* Eli Lilly & Company.

is 16 Gm. in 200 cc. of water three times daily, a total of 48 Gm. in 24 hours, 15 to 30 minutes before meals, but larger amounts may be required. I have allowed a fluid intake of 1500 to 1800 cc. daily. A 3.75- to 4-Gm. salt diet is prescribed, which is roughly a normal diet as cooked with no extra salt added while eating. Serious electrolyte disturbances have not been encountered. Many patients experience no undesirable side effects. A few patients complain of constipation. The older patient, who beforehand suffers from constipation, may present difficulty. In a few patients the drug has had a mild cathartic effect. In certain patients with chronic congestive heart failure the resin has appeared to promote diuresis, to enhance the diuretic effect of mercurial drugs, and to allow a more satisfactory state of compensation to be maintained, and also to permit fewer mercurial injections. The place of resins in the treatment of cardiac failure has not yet been defined.

Oxygen

Oxygen should be used promptly when there is marked cyanosis and respiratory distress. It makes breathing more comfortable; cyanosis may disappear. As a consequence, the patient is able to relax and fatigue is lessened. Oxygen may also induce diuresis. This has been demonstrated in patients with heart failure who have been kept in an oxygen chamber for long periods of time. Oxygen should not be given over prolonged periods to patients in whom congestive heart failure results from certain forms of pulmonary heart disease, such as emphysema (see Chapter 16).

The rationale of the use of oxygen is as follows In most instances of congestive heart failure the cardiac output is decreased and the velocity of blood flow is retarded. More oxygen is removed from each unit of blood than under normal circumstances Consequently the mixed venous blood collecting in the right side of the heart has a greatly lessened oxygen saturation When this unsaturated blood passes through the lungs, it does not attain the normal saturation of approximately 95 per cent, partly because of its initial unsaturation, but mainly because pulmonary congestion interferes with adequate oxygen exchange (in the absence of pulmonary congestion slow circulation may in fact permit a higher oxygenation). The therapeutic use of oxygen pushes more oxygen across the barrier of pulmonary congestion and the blood may become normally saturated. This normally saturated arterial blood does not drop to the former level of unsaturation prevailing when distributed to the tissues, although the same amount of oxygen may be extracted by the tissues from each unit of blood

Under most circumstances the oxygen *tent* is satisfactory. Many patients object to the discomfort of the face mask but oxygen may be given by this method when it is the only means available; it may be used as an emergency measure until a tent can be secured. Oxygen may also be given less effectively by a nasal catheter.

A patient's anxiety about the oxygen tent may be allayed by a proper explanation of the reason for its use Formerly many patients complained of being shut in, but the transparent tents which are now available are acceptable to most persons

Technic

The air inside the tent should be kept cool, adequate circulation should be maintained, an oxygen percentage of approximately 50 maintained, and the carbon

dioxide removed from the expired gas before it is recirculated. Proper warning should be given about smoking, sparks, and electrical apparatus in the room. The administration of oxygen is discontinued gradually after the patient has improved. When possible, patients should be given brief trials without oxygen before it is finally discontinued. In this way the use of oxygen is discontinued over a period of 24 hours. It may be expedient to have the patient sleep in the tent at night over a prolonged period, breathing room air in the daytime. In severe congestive heart failure with limited reserve, when expense is not important, the oxygen tent may be used with benefit at night over long periods of time.

Sedatives

Morphine

Where dyspnea is very marked and the patient is restless and uncomfortable, morphine usually provides prompt relief and sleep It may be given in 15-mg. amounts by mouth or by hypodermic injection when oral administration is not feasible because of nausea and vomiting and when immediate relief is necessary. It may be repeated in three to four hours. This drug may be required for perhaps a day or so while the patient is very sick and while diuretics are taking effect. Care should be exercised that addiction does not ensue. If morphine induces nausea and vomiting, pantopon or perhaps dilaudid (3 mg) may be substituted. When morphine or codeine are used special care should be taken to prevent constipation (p. 6). Patients should be turned frequently in order to prevent stasis at the lung bases which may lead to hypostatic pneumonia. Morphine and demerol (50 to 100 mg) may have an antidiuretic effect in some patients, and may account for the lack of diuresis from mercurial drugs in certain acutely sick patients.

Codeine

Fifteen to 30 mg. of codeine may be used for cough when morphine is not being given at the same time. This drug may be used with aspirin for pain It is better to use codeine for cough in tablet form than to include it in one of the cough mixtures; these are usually sweet and may cause nausea

Others

Chloral hydrate 0 3 to 1 0 Gm., triple bromides 1.0 Gm., or phenobarbital 15 mg two or three times a day may be used when patients are anxious and restless.

MECHANICAL MEASURES

Phlebotomy

There are only a few occasions (see p 28) when phlebotomy is required. If the venous engorgement is extreme and the patient is markedly cyanotic and in a critical condition, phlebotomy may give a measure of immediate relief before the medication can take effect One-half of a liter of blood may be removed quickly through a large-bore needle with a tourniquet on the arm Even though the blood volume is increased in congestive heart failure, its restoration following phlebotomy

is accomplished by drawing fluid from the tissues into the blood stream. As a result, during the next 24 hours the blood is diluted and the red blood cell count is lowered; these two factors may throw an additional burden on the heart. Nevertheless the immediate gain may outweigh these consequences. If phlebotomy is indicated and a needle is not available it may be expedient to cut down upon the vein with a scalpel, or with a razor blade.

The cardiac output, as we have stated earlier, is decreased in the presence of the most common types of congestive heart failure—the so-called "low-output" failures. Howarth, McMichael and Sharpey-Schafer have shown that the cardiac output increases following venesection in low-output heart failure Phlebotomy lowers the venous pressure (and accordingly the right auricular pressure) and increases the volume output from the heart. The clinical benefit which follows phlebotomy is to be attributed to the improvement in cardiac output.

The application of tourniquets to the four extremities may be beneficial in acute heart failure. Blood pressure cuffs may be applied to each extremity and the pressure raised to a level to cut off peripheral venous return but not to obstruct arterial flow. One limb may be released in rotation every 15 to 20 minutes. Tourniquets trap some of the circulating blood in the extremities and spare the heart the burden of pumping the volume of blood which is diverted

Thoracentesis

I do not remove fluid from the chest by paracentesis unless the pleural effusion is massive and dyspnea is marked. If the patient is seriously sick thoracentesis may be a trying procedure, as is shown by the occasional death from pleural shock It may be more important in the long run to inaugurate the other measures and allow the patient to rest As the patient improves and diuresis begins, pleural effusion gradually disappears and the patient is not deprived of the proteins which the fluid contains In the long run the mechanical removal of fluid from the pleural cavity does not diminish the time required for restoration of compensation.

When thoracentesis is contemplated, *morphine or codeine should be given long* enough beforehand to make the patient comfortable. Local anesthesia of the skin and deep tissues should also be provided with procaine Care should be exercised not to induce a pneumothorax Not more than 1000 cc. to 1500 cc. of fluid should be removed at one time. It is unwise to remove fluid from both sides of the chest on the same day, unless this is absolutely necessary.

There are two groups of patients who may require thoracenteses every few months: (1) patients with chronic heart failure who do not respond to medical treatment; and (2) ambulatory *patients who cannot* be kept free of failure because there is gradual accumulation of fluid beyond the amounts which the therapeutic measures dissipate, and because it is not possible to give them prolonged bed rest either in the hospital or at home.

The slow rate of dissipation of fluid from serous cavities by medical means should not cause impatience. If fluid persists in one or both pleural cavities after an ample exhibition of medical measures, its removal by tap is then in order if it causes discomfort or dyspnea, or impairs respiratory function.

Paracentesis Abdominis

If diuresis occurs promptly after the institution of mercurial and digitalis therapy and the whole therapeutic regimen, enough fluid is drawn away from the abdominal cavity to relieve the abdominal tension and cause the ascites to disappear. This medical removal of the fluid is, I believe, preferable to the surgical, as it does not deprive the patient of the proteins which the fluid contains. I have not been impressed that diuresis occurs after paracentesis abdominis or that mercurial diuretics are more effective after removal of ascitic fluid.

When ascites either is not relieved by diuretics or reaccumulates after removal by tap at a pace which diuretics will not control, abdominal taps are indicated. The flow should be stopped every few minutes to allow the splanchnic circulation to adjust to changing pressures. Patients may faint because the sudden lowering of intra-abdominal pressure and the pooling of blood in the splanchnic area deprive the brain of adequate circulation.

The patient should be made comfortable before tap by the use of morphine or codeine. Good procainization of the area should be attained before inserting the trochar. If the patient is not too sick, he should sit on the edge of the bed with the legs over the side and the feet resting in a chair or on a stool. He is then ready to lie back in bed should untoward symptoms occur. The patient may also sit in an armchair. This position may be useful if frequent paracenteses are required and the patient is adjusted to the procedure.

The likelihood of continued leaking from the trochar opening for some days, with constant wetting of the clothing and bedclothes and resulting irritation of the skin, is one drawback of paracentesis Oozing results frequently from inadequate suturing of the paracentesis opening. Under these conditions the benefits are outweighed by the inconvenience which accompanies it, as well as by the risks of infection.

The implantation of a Murphy button or a tube with sievelike openings connecting the peritoneal cavity with the subcutaneous tissues has not been effective in continuous drainage of ascitic fluid.

Southey Tubes

The Southey tube is a large phlebotomy needle with sievelike holes punched in the shaft. The tube is inserted for several centimeters in the edematous subcutaneous tissues and left in place. A rubber tube is attached to the exposed end of the tube so that the fluid may drip into a container. Tissue pressure forces the edema fluid through the sieve openings. Penicillin may be used to prevent local infection of the skin. Several liters of fluid may be removed by this means in 24 hours. Several tubes may be inserted in each leg. Removal of edema fluid by the use of Southey tubes was more common formerly than it is now. This is an uncomfortable form of treatment and with the introduction of newer drugs for the treatment of heart failure, Southey tubes are rarely required at the present time.

Dialysis of Salt from the Body

Cherkasky and Hellman have applied the dialysis technic of Darrow and Yannet to the removal of sodium chloride from the body. Several liters of 5 per cent glucose are instilled into the peritoneal cavity after the withdrawal of ascitic fluid. The glucose solution is allowed to come into equilibrium with the blood for two and one-half to four hours. In this process sodium chloride is removed from the blood and enters the fluid in the peritoneal cavity. At the end of the allotted time the glucose solution is removed from the peritoneal cavity, and with it a large amount of sodium chloride. Diuresis follows in the next 48 hours as the kidneys excrete the water from which the sodium chloride has been removed.

This form of therapy is in the experimental stage. It should not be attempted in patients who are only slightly edematous or who are dehydrated It is obviously not a practical procedure for the treatment of heart failure.

TREATMENT OF SYMPTOMS

There are many measures which do not have any specific part in the diuretic program but which eliminate or decrease certain symptoms. When the liver is greatly swollen and tender, the application of a flaxseed poultice may provide immediate relief. The use of a rectal tube and the application of warm turpentine stupes also may give prompt relief from abdominal distension Turpentine stupes, or course, must not be used during oxygen therapy.

Patients must not use sodium bicarbonate for indigestion or other gastrointestinal complaints The addition of sodium in this form may nullify for several days all the attempts to restrict sodium in the diet. One of the aluminum hydroxide preparations may be used instead of sodium bicarbonate.

MEASUREMENTS TO BE MADE

Weight

The daily weight of the patient in the morning before breakfast is a useful guide to the effect of treatment (Figs. 1, 2, and 13) If the patient is weighed every two or three days instead of daily, the fluctuations may be so great that they cannot be correlated with the effect of medications For the patient who is very ill weighing is not possible unless stretcher scales are available, but harm need not result from weighing the patient at the bedside if he is not too dyspneic. As improvement occurs the patient may be allowed to use the commode at the bedside while up for weighing Ambulatory patients can weigh themselves daily and keep a record for the physician. A patient may have good reasons for either gaining or losing weight: He may lose edema and other fluid accumulations, with improvement in the circulation and with an increased food intake, there may be a tendency to gain weight.

Urine Output

Accurate comparison of the urine output with the fluid intake for each 24-hour period affords a graphic account of the effect of diuretics which the weight curve

alone does not supply (Figs. 1, 2, and 13). Although some fluid is lost as sweat through the skin, as moisture in the stools, and as moisture in expired air from the lungs, this is not a valid argument against measuring that part of the daily loss of fluid which is so readily and easily measured as urine. Ambulatory patients can be trained to measure their own urine output—at home or in the hospital—without any undue heart consciousness. When the patient is being treated at home a member of the family can be shown how to keep account of the volume of urine.

Pulse Deficit

Simultaneous apical heart and radial pulse rates should be counted if possible *every four hours* when the patient with auricular fibrillation is awake and oftener if necessary during the period of digitalization. Slowing of the ventricular rate and decrease in the pulse deficit not only are excellent guides to the progress of digitalization; they also aid in selecting the amount of digitalis which should be prescribed next. The rates should be counted after the patient has rested. They should not be recorded immediately after meals, or ambulation, or while the patient is moving around in bed. The effects on the heart rate and pulse rate of exertion or sitting up can be ascertained by appropriate observations.

When treatment is carried out at home without nurses, a member of the family usually can be trained quickly to count the apex thrust and the radial rate To some patients a stethoscope may be supplied. I have certain patients exhibiting chronic auricular fibrillation who have become very adept at managing their digitalis dosage without morbid interest and without concern. When normal sinus rhythm is present, counting the radial rate is sufficient unless irregularity occurs. As signs and symptoms of heart failure regress and digitalis becomes effective, the heart rate in the presence of normal rhythm declines in most patients. The slowing is not, however, so dramatic as in patients exhibiting auricular fibrillation.

MOBILIZATION

If there are no contraindications after the objectives of bed rest have been achieved (see p. 4) the patient is ready for slow mobilization, during which the same schedule of medications is maintained. There are two reasons for slow, progressive mobilization (1) in order not to overburden the heart which has failed and is now restored to compensation, (2) in order to establish the functional capacity of the patient.

The patient sits on the side of the bed once or twice the first day for 15 minutes with his feet in a chair, the patient with heart failure has usually been propped up in bed and does not have to become adjusted to sitting upright again On the second day the patient is allowed out of bed in a chair at the bedside for 15 minutes in the morning and, if there is no undue fatigue, for 15 minutes again in the afternoon. He is observed while sitting up and after return to bed for fatigue, effect on heart rate, dyspnea, or any other evidences of distress

The schedule on page 24 can be used as a basic pattern, to be slowed if the patient's reaction warrants it Some increase in mobilization should, however, be achieved every day

1st day:	patient sits up	15 min.	in the A.M. and	15 min.	in the P.M.
2nd day:	" " "	30 "	" " " "	30 "	" " "
3rd day:	" " "	45 "	" " " "	45 "	" " "
4th day:	" " "	1 hour "	" " "	1 hour "	" "
5th day:	" " "	1½"	" " " "	1½"	" " "
6th day:	" " "	2 "	" " " "	2 "	" " "
7th day:	" " "	2½"	" " " "	2½"	" " "

When the patient is sitting up five hours a day this time is kept constant and walking is allowed. At first a few steps are allowed several times during the day; the next day the patient may move around the room, the next day he may walk around the room more or may venture out of the room; from this point on there is a gradual daily increase in the distance. In a hospital, lengths of corridors are useful measures.

After beginning to walk the patient may go to the lavatory during the time he is sitting up. After about one week of the walking schedule and two weeks after the patient began sitting up, a tub bath or shower may be allowed. During this time the patient has of course been kept on the regimen which has been used during the period of bed rest and close watch is maintained for signs and symptoms of recurrence of heart failure. If signs of decompensation recur during mobilization a more rigid regimen is indicated, and the patient may have to decrease his activity or remain in bed a day or two for the signs of failure to regress. After this, mobilization is undertaken even more slowly. At times it may be necessary only to increase the frequency of mercurial injections if they are being given less often than every third day.

With increased activity the strength of the patient usually returns. The patient feels the buoyancy of progression which is not possible if mobilization is undertaken more rapidly with the possibility of a setback. When the patient has been treated in a hospital it is wise, if possible, to have him caring for himself by the time he is discharged unless adequate nursing care can be provided at home, but he should be kept on the hospital regimen for a few days before any increases in activity are permitted. At this stage the length of time the patient is allowed up is increased to six hours daily for a while, then to seven hours, after which gradual additions are continued. If it is necessary to climb stairs at home it may be best for the patient to be far enough along in mobilization to accomplish this before discharge from the hospital. Two or three steps can be tried the first time, with gradual addition of a few steps until the number is reached that the patient has to use. Stairs should be climbed slowly.

On discharge from the hospital, diet, fluid intake, activity, and medication should be carefully discussed with the patient and his family. Giving exact written directions facilitates compliance with the regimen and avoids errors. Unless these are given and followed the whole period of hospitalization may be wasted Stress should be laid on keeping to the regimen and on returning to the office or clinic for mercurial injections.

Until the patient has over many weeks or months reached the maximum activity which is advisable, each increment of activity should be guided by the physician and not left for the patient to manage with the advice "not to do too much." One

is amazed at the frequency with which patients on recovery from heart failure are discharged from the hospital without medication because they were free of symptoms and signs at the time of discharge, only to return to the clinic or to the private doctor ten days or more later in as severe a state of heart failure as before.

Decision must be made by the physician about returning to work: whether it is possible at all; how the patient can get to work without climbing stairs or with minimal stair climbing; and whether the patient's occupation is compatible with his heart disease and with his functional capacity. Thoughtful employers can often shift an employe to lighter work which the patient can do efficiently. Arrangements can frequently be made for the patient to work part time at first until his functional capacity has been tested and adjustments are made to reemployment. After this the patient is ready for a longer day.

During this time under medical supervision, modifications of the regimen and medications might be required.

AMBULATORY TREATMENT

Ambulatory treatment may be indicated because of economic reasons; or patients may refuse to remain in bed or to be admitted to a hospital, or hospital beds may not be available. Apart from these considerations, the physician may decide that an ambulatory regimen may be adequate if failure is not too severe and if the patient has neglected or has not previously had any of the accepted forms of therapy in a well-coordinated program. With cooperative patients restriction of fluid intake, the low salt diet, the mercurial regimen, ambulatory digitalization, and the amounts of rest and activity which appear indicated, all can frequently be satisfactorily managed in a schedule which will result in restoration of compensation. But even when the decision is made to carry out a trial period of ambulatory treatment, it should be kept in mind that many patients suffering from heart failure have the maximal cardiac output at rest that their hearts can attain.

REDUCTION OF BASAL METABOLIC RATE

Thyroidectomy

Thyroidectomy for chronic congestive heart failure has been advised in order to reduce the metabolic requirements of the body so that the demands upon the heart could be lessened in patients who could not be restored to compensation, as well as for those incapable of activity without the recurrence of heart failure. It was found that total thyroidectomy was required to induce a state of myxedema. If any thyroid tissue was left its secretion of thyroid hormone increased to keep the basal metabolic rate near the normal level. Patients subjected to this procedure were presumably those with normal thyroid activity. The basal metabolic rate however is not uncommonly increased as a manifestation of heart failure (Stewart and Jack).

This form of therapy had a short vogue and has practically been abandoned. The induction of a permanent disease such as myxedema with its own complications discouraged physicians from treating many patients in this fashion. When

patients have complete surgical thyroidectomy the same benefit may not accrue from the use of thyroid extract as replacement therapy, as is the case in spontaneous myxedema. Physiologically there is another reason for not recommending this procedure. It has been pointed out that in most instances of congestive heart failure the cardiac output is decreased, the velocity of blood flow retarded, and the heart dilated (Figs. 15 and 16) (Stewart et al). On the other hand the cardiac output is also decreased, the circulation time prolonged, and the heart large in myxedema (Figs. 42 and 44) (Stewart et al.). To superimpose these two similar conditions on the functional capacity of the heart would not appear to promise improvement in the cardiac condition.

Naturally thyroidectomy or the use of antithyroid drugs is indicated in patients with heart failure who have evidence of hyperthyroidism.

Antithyroid Drugs

Propylthiouracil

There are some patients in whom the basal metabolic rate is elevated by 10 to 20 per cent or more during heart failure in the absence of hyperthyroidism (Stewart and Jack). If the basal requirements could be slightly reduced without inducing a myxedematous state such a patient might be benefited. *Propylthiouracil* may be used for this purpose. Instances of toxic effects in the therapeutic range of dosage of this drug are few, so that there is not a great risk in giving it a trial in patients with stubborn congestive heart failure. Reducing the basal metabolic rate from +10 or +25 per cent to −10 per cent may be sufficiently sparing of the heart to achieve compensation more easily or allow a slightly higher level of activity on the part of the patient. Propylthiouracil is given as described in Chapter 14. Reduction of the basal metabolic rate to −10 or even −15 per cent should be the aim Account should be kept of the serum cholesterol, the basal metabolic rate, and the white blood count Patients receiving propylthiouracil should report to the physician immediately any change in the state of well-being. The same care should be exercised as with patients receiving the drug because of hyperthyroidism. The drug may not succeed in lowering the basal metabolic rate in euthyroid individuals.

Radioactive Iodine

Radioactive iodine in the treatment of chronic congestive heart failure is discussed on p. 291 and on p. 331.

PULMONARY EDEMA

Pulmonary edema is usually of sudden onset. It is characterized by the extravasation of fluid from the circulating blood into the alveoli, bronchioles, and bronchi The main clinical manifestations are dyspnea, cough, distension of the neck veins, and the expectoration of pale pink, frothy, watery sputum. It is characterized by fine to coarse râles throughout the lung fields. The mechanism of acute pulmonary edema is not known.

Although pulmonary edema results commonly when a damaged heart is subjected to acute or prolonged stress (as by exertion), it may result from sudden

decrease in the functional capacity. Pulmonary edema occurs under widely diverse circumstances; it may follow the inhalation of irritating gases, cerebral accidents, fractures of the skull, phenobarbital poisoning, and shock. It is seen most commonly in patients with myocardial damage, especially in the presence of hypertension, in arteriosclerotic heart disease, in coronary artery disease, and in acute coronary thrombosis. It is also seen in patients with rheumatic heart disease, in whom it may be precipitated by acute respiratory infections. It may be precipitated by the onset of paroxysmal tachycardia, auricular fibrillation, or auricular flutter. It may result from overdistention of the circulation by intravenous fluids.

Immediate Measures

The patient should be put to bed, propped up in the most comfortable position. Morphine 15 mg. should be given at once by hypodermic injection, to quiet breathing and to allay apprehension. *Aminophyllin* 0.24 to 0.48 Gm. is given intravenously, and may be repeated in one hour if necessary. The injection should be given very slowly, over a period of four or five minutes. If the patient experiences distress the injection can be interrupted at once. Sudden death following the intravenous administration of aminophyllin has been reported, and probably resulted from cardiac standstill or ventricular fibrillation.

Aminophyllin induces its benefit by increasing the cardiac output, probably by a direct action on heart muscle, and by lowering the venous pressure. Stewart and Jack showed that aminophyllin given intravenously increased the cardiac output. Howarth, McMichael and Sharpey-Schafer confirmed this observation in more extensive observations carried out with the technic of right auricular catheterization. They found that it is the theophylline part of the drug which is responsible for increasing the cardiac output and bringing about a rapid fall in right auricular pressure. These effects are apparent within a few minutes after injection.

Digitalization

If the patient has not been digitalized or has not had digitalis within two to three weeks a digitalis effect should be induced as rapidly as possible. To this end, ouabain 0.5 mg. or lanatoside C may be given intravenously at once. The full digitalizing amount of 1.6 mg. of lanatoside C may be given at one injection, which is excreted within 72 hours. This is probably the drug of choice at the present time. Maximal effects following its intravenous use are apparent in one-half to three hours.

If one of the foregoing preparations is not available digitoxin 1.2 mg. may be given intravenously. Digitoxin of course acts more slowly; its effects begin in approximately one hour but its maximum effect is not attained for many hours. Adequate digitoxin is given later to complete digitalization, up to a total of 1.8 mg. It may be the safer procedure to give 0.8 mg. as the first dose and 0.4 mg. one to two hours later. Even with this extreme caution abnormal rhythms may result. If preparations for intravenous use are not available, a preparation of whole leaf, digitoxin, or digoxin may be given orally. If the patient is partially digitalized when pulmonary edema occurs, digitalization should be completed but care is

exercised not to induce toxicity. The preparations of digitalis and the dosages are described fully in Chapter 3.

Oxygen

If the patient is in a hospital when pulmonary edema occurs, oxygen may be given at once by mask until a tent is available. In certain instances oxygen is given by mask under a positive pressure of 3 to 4 cm. of water in order to try to prevent the escape of fluid from the blood into the alveoli. Helium and oxygen may be given under a positive pressure of approximately 5 cm. of water.

Antifoaming Agent

The movement of air in the bronchi and alveoli in pulmonary edema whips the fluid which has been extravasated into a foam which interferes with the exchange of oxygen and carbon dioxide across the alveolar wall. The studies of Luisada relating to the use of antifoaming agents in the treatment of pulmonary edema have been put to clinical test by Gootwick and Luisada in the use of the inhalation of ethyl alcohol vapor in oxygen under pressure. This is achieved by having oxygen from the oxygen tank bubble through a bottle half filled with 50 per cent ethyl alcohol. The alcohol bottle has in its stopper two large-bore metal tubes. One of these tubes reaches to the bottom of the bottle and carries oxygen which bubbles through the alcohol; the other tube is above the fluid alcohol level and carries the alcohol-bearing oxygen over to the meter mask, without appreciable loss in pressure. Clinical improvement has followed the use of this method, without adverse systemic effects of the alcohol. In high concentrations the inhalation of ethyl alcohol vapor would be expected to give rise to cerebral manifestations of intoxication.

Mercurial Diuretics

Two cubic centimeters of one of the mercurial diuretics may be given intravenously. In this instance it is better to use the drug intravenously to assure a more rapid response than to give it intramuscularly or subcutaneously.

Phlebotomy

I rarely resort to a phlebotomy to decrease the blood volume. If the patient's condition is grave 200 to 500 cc. of blood may be removed The lowering of blood volume by the phlebotomy is made up rather promptly by drawing tissue fluid into the blood stream.

Tourniquets

Tourniquets applied to the extremities trap blood in them. This procedure may relieve the heart of the burden of pumping the amount of blood which is temporarily removed from the circulation.

Glucose

I do not recommend the use of 50 cc. of 50 per cent solution of glucose intravenously. The hypertonic solution draws fluid from the tissues into the blood stream and increases the blood volume. This places an additional burden on the heart.

Atropine

I do not think that atropine in 0.0006-Gm. to 0.0012-Gm. amounts is of any benefit If given in adequate amounts to induce clinical atropine effects, such as dryness of mouth, it may increase the heart rate to such an extent as to be harmful. Increasing the pace of an already overworked heart which has failed acutely does not appear to be a good therapeutic measure.

Continued Treatment

By the use of morphine, aminophyllin, digitalis, and oxygen, the respirations become quieter and slower, the venous engorgement lessens, the amount of sputum decreases, the râles become fewer so that the chest may be clear within a few hours, the heart sounds, which were faint and also obscured by the respiratory noises, become louder and acquire a better quality. As the acute stage passes digitalization is completed if it has been only partially accomplished; the fluid intake is restricted. A soft diet is given for a few days, followed by a more liberal diet which is low in salt.

Bed Rest

The patient should be kept in bed to allow for accumulation of cardiac reserve. The duration of bed rest varies with the rapidity of the clearing of the pulmonary edema, with the basic cardiac damage, and with the circumstances under which the pulmonary edema occurred. For instance, pulmonary edema occurring in the course of coronary thrombosis would require prolongation of bed rest until healing of the myocardial infarction had been assured. On most occasions mobilization may be more rapid than in the usual case of heart failure exhibiting edema and other signs of decompensation.

Digitalis

When pulmonary edema occurs in a patient with cardiac disease digitalization is maintained by ration doses together with the usual regimen of a patient who has suffered heart failure. These measures may not be necessary if pulmonary edema took place under conditions which need not recur. Paroxysmal tachycardia would be such an instance. For patients who suffer from repeated attacks of pulmonary edema injections of mercurial diuretics at regular intervals are frequently a good preventive measure. Patients should learn to live within the capacities of their hearts and to avoid sudden or prolonged exertions.

NOCTURNAL DYSPNEA

Dyspnea may be associated with exertion or be present at rest as a manifestation of heart failure. It may be so severe that the patient cannot lie down, but has to sit up in order to breathe; in short, the patient is orthopneic In certain patients, however, dyspnea is paroxysmal in type or occurs at night. When it follows this last pattern it is called nocturnal dyspnea

Paroxysmal and nocturnal dyspnea constitute what is often called *cardiac asthma*. In many instances the respiratory distress is associated with wheezing, and musical

râles may be heard in the chest during the attack. Even though the term "cardiac asthma" describes the clinical picture, I rarely use it because it may be confused with the usual type of asthma associated with allergy.

Frank pulmonary edema may be an accompaniment of nocturnal dyspnea. The *sequence of events may be as follows:* The patient falls asleep comfortably, perhaps propped up in bed on pillows. While asleep he slides down so that he now lies flat. Some while later he awakens complaining of difficulty in breathing. He must sit up in bed to catch his breath. There may be audible wheezing and the patient may have the impulse to rush to an open window to "get air." On examination there may be moist râles at the lung bases or over the posterior chest if the patient has been lying flat. There may be musical snores and wheezes throughout the chest. At other times there are fine to coarse râles throughout the lung fields, in short, the picture is that of acute pulmonary edema. Such a patient may recover with amazing rapidity on sitting upright in a position which enables him to breathe more easily.

Nocturnal dyspnea occurs most commonly in patients with hypertensive and arteriosclerotic heart disease, with coronary thrombosis, and with aortic insufficiency. Attacks are usually associated with severe myocardial disease.

Morphine, intravenous aminophyllin, oxygen, digitalis, and mercurial diuretics are used as in the treatment of pulmonary edema, if they are available or if the patient is in the hospital. If the patient suffers attacks at home, morphine should be available for immediate use. When these occur with sufficient frequency in patients who are at home, provision may be made to have certain measures such as oxygen available for immediate use. Aminophyllin 0.2 Gm. orally or as a 0.5 Gm. suppository at bedtime may forestall attacks. Rigid adherence to a mercurial diuretic schedule may prevent their occurrence. Attacks may be transient. Patients may experience complete relief without any residual discomfort as soon as the attack has passed.

SURGICAL MEASURES FOR VALVULAR DISEASE

The application of surgical measures to the treatment of patients with chronic congestive heart failure due to valvular deformity is discussed in Chapter 7, p. 231

AMBULATORY TREATMENT AFTER RECOVERY FROM CONGESTIVE HEART FAILURE

Most patients who have suffered from congestive heart failure require the continuation of some sort of regimen after recovery and after reaching their maximal functional capacities. In a few instances the patient may return to leading a normal life as long as excesses are avoided. This may be the case when heart failure has occurred under unusual circumstances which need not recur, such as surgical operations, paroxysmal tachycardias, acute infections, acute rheumatic fever, and pregnancy.

Upon recovery from first attacks of congestive heart failure many patients may be kept free of recurrent decompensation by proper management of activities and of medical therapy. The schedule must be individualized for each patient.

Most patients should be kept on a limited fluid intake: 1200 to 1500 cc. daily. It may be sufficient to limit the salt intake to that used in cooking. In other patients more stringent restrictions require that the food be cooked without salt and the patient's portions removed before seasoning those of the rest of the family. The use of salt-free bread and butter may be necessary. In other instances the strict adherence to an 0 5- to 2 0-Gm. salt diet is necessary if recurrence of fluid accumulations is to be prevented. Many patients manage on a regimen of reduced fluid and salt intakes and maintenance doses of digitalis. These maintenance doses should be continued, instruction being given about the appearance of toxic symptoms. Other patients may require mercurial injections once or twice a week A certain number of patients requiring mercurial diuretics regularly may be taught to administer their own subcutaneous injections of thiomerin, just as diabetic patients administer their own insulin, and return to the clinic or their physician at intervals of two to four weeks. In others still, ammonium chloride may be required. Certain of the other diuretics may be used with digitalis or in addition to the mercurial Patients in whom fluctuations in urine volume do not occur, such as those given digitalis only, need not measure the urine output, but should watch the daily weight.

Patients seen by their physicians at infrequent intervals should be advised to seek an appointment when there is any change in their state, such as a gain in weight or the appearance of new symptoms or of any complications Care of respiratory infections is important. Patients may become adjusted to their ambulatory regimen and remain in a good state of compensation until an attack of acute bronchitis increases the load on the heart. The special problems which present themselves in treating heart failure resulting from rheumatic heart disease are discussed in Chapter 7. Treatment should be supplied for the underlying cause of the heart disease.

The objective in the treatment of congestive heart failure should be to keep the patient free of evidences of heart failure and then to add on as much activity as can be tolerated without the recurrence of decompensation. The goal should be for the patient to remain free of failure on his regimen or to exhibit only a few râles at the lung bases, with a slight gain of weight between mercurial injections—all of which signs disappear promptly after the next mercurial injection. In certain patients this ideal cannot be maintained and adjustments must be made in their management. As there is not enough hospital space available to take care of all cardiac cases, patients may have to remain ambulatory and work while they have evidences of moderate heart failure. The best possible regimen with respect to activity, diet, and mercurial schedule is worked out for each patient. Many carry on satisfactorily for many months with gradual increase in signs of heart failure, and with readmission to the hospital at intervals of about a year for a period of bed rest, or briefly for thoracentesis or abdominal tap In other patients more frequent taps may be necessary.

Patients who can restrict their activities may be able to maintain compensation if they remain at rest in bed one-half of the day and are active the remainder of the day. For other patients one day a week may be made a complete rest day. Patients feel better and maintain a happier attitude if they have some freedom of

activity while they are up, than if they are up and down all day long, in and out of bed, and do not feel well any part of the day. It is a good plan to have patients rest ahead of time to meet some unusual demand rather than to try to catch up afterward. For instance, patients wishing to go out in the evening should rest in the afternoon.

With care and cooperation on the part of the patients and with effective thera- [illegible] upon their most productive years during this period, when constant medication and supervision are required. Physicians can encourage patients by recounting to them the cases of patients who have done very well, thus providing objectives at which to aim. In other patients all may go well from the point of view of the cardiac status until an intercurrent disease causes death.

The cardiac pattern, however, may be somewhat as follows: As time goes on, either because the basic lesion progresses or because of stress, heart failure recurs. With the passing of years, the crescendo of recurrences of heart failure builds up. Attacks become more frequent and more severe until complete bed rest and the use of all the measures which are available are no longer effective in restoring compensation. Pleural or abdominal taps are required more frequently to give a measure of relief of symptoms In the presence of auricular fibrillation in the terminal stage of heart failure it may not be possible to give sufficient digitalis to keep the ventricular rate slow. Ventricular premature contractions and coupled rhythm appear as digitalis is increased (see Pronestyl, p. 178). Here a compromise is made in the amount of maintenance digitalis between that which will give the optimal ventricular slowing and that which causes the fewest premature contractions. In the terminal stages of heart failure treatment is directed toward the relief of symptoms and of complications. Active use of all the measures available for the treatment of congestive heart failure are employed. The physician's optimism about the outcome must be maintained for the patient's encouragement.

SUMMARY

In the minds of most lay persons heart failure and the use of digitalis carry a bad prognosis. Efforts should be made to allay this apprehension. Patients may have a single episode of heart failure under circumstances which need not recur. In other patients this manifestation may be indefinitely delayed as a first occurrence, or after the first occurrence subsequent attacks may be indefinitely postponed, by institution of suitable regimens and by sincere cooperation of the patients in the regimens. The patient must be made to see that it is a joint effort with the physician and that complete reliance cannot be placed on medications to relieve the harm done by indiscretions. The outlook may not be bleak even in patients who require constant supervision, nor in those who must have mercurial injections as frequently as once or twice a week in order to maintain compensation. Such patients may remain self-supporting and carry on their professions without increasing the hazards and without altering the outlook for the worse. Certain of those patients come to be an inspiration to the physician Because of their mainte-

nance of spirit and courage, they serve as stimuli to seek better means and drugs for treating this phase of heart disease. The patient with congestive heart failure has at present a much better outlook than was offered not so many years ago the improved effectiveness and safety of mercurial diuretics, the wider recognition of the need for a strict low sodium diet; the use of digitalis in adequate amounts; the introduction of various digitalis preparations which lend themselves to special uses, the introduction of new chemotherapeutic agents to combat infections which were formerly formidable or fatal to patients with heart disease, the early and frequent use of oxygen—all these have contributed to a better prognosis

It is hoped that the recent published studies which have advocated the use of large amounts of fluids or fluids ad libitum in the treatment of heart failure will not have an adverse effect on the treatment of these patients. In our experience a limited fluid intake remains an integral part of the regimen in taking care of patients with congestive heart failure.

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CHAPTER 2

Mercurial Diuretics

HISTORY

Most patients with congestive heart failure today are given one of the mercurial drugs in order to induce diuresis. These may be required transiently in order to aid in the restoration of compensation, or their continued use may be necessary to maintain it. Early in the development of mercurial drugs *novasurol* and *salyrgan* were introduced, the former as a mercury compound for the treatment of syphilis It was found by accident that it induced diuresis, a phase of study which was promptly and fruitfully amplified.

A further advance in the development of mercurial diuretics was the discovery that combining them with *theophylline* not only reduced the local toxic effects but also resulted in more effective diuresis. Moreover DeGraff found that the addition of theophylline lessened the local reaction produced by intramuscular injection of these drugs.

ACTION

On the basis of tracer studies with intravenous mercuhydrin labeled with radioactive mercury, Burch showed that mercury leaves the blood stream rapidly and that it is distributed through the body in every organ. The metal is found in greatest concentration in the kidneys but the liver acquires a total of three times as much because of its size.

Mercury given for diuresis is excreted completely in 48 to 72 hours. Seventy-five per cent or more is recovered in the urine and feces in that period. The excretion is greatest immediately after injection and during marked diuresis. The addition of theophylline increases excretion by 30 to 40 per cent (DeGraff). Grossman et al. found that 60 to 95 per cent of the injected mercury was excreted

in the urine in the first 24 hours after the injection of thiomerin subcutaneously or intravenously and of mercuhydrin intramuscularly in 2-cc. amounts. Fifty per cent was excreted within three hours; the fecal excretion ranged from 1 to 2 mg. per day for a few days after injection.

The mercurial diuretics induce diuresis by reducing tubular reabsorption of water. Increase in glomerular filtration does not result. The urinary excretion of chlorides is greatly enhanced by the mercurial diuretics There is also increased urinary excretion of sodium, potassium, and calcium. In most patients long use of mercurial diuretics does not damage the kidneys so far as can be detected from measurements of renal function.

Pugh and Wyndham found that the intravenous injection of mercurial diuretics caused a rise in cardiac output and a fall in right auricular pressure. These effects were apparent two hours after injection and reached a peak in five to seven hours. The effects waned with the return of urine output to normal. They suggested that the changes may be due to fall in blood volume. Those mercurial diuretics containing the theophylline radical caused an additional transient rise in cardiac output and fall in right auricular pressure

INDICATIONS

I do not recommend the use of mercurial diuretics for every patient suffering from congestive heart failure Rest in bed, a low salt diet, restriction of fluid intake, and digitalis may be adequate to induce diuresis and restore compensation (Figs. 13 and 14). Only if these measures do not affect prompt diuresis is the use of a mercurial diuretic indicated. Current practice has tended to include the use of mercurial diuretics in all cases of heart failure and to regard it as routine for the maintenance of compensation. There is a tendency to give so many drugs at the same time that neither the benefit from each nor the necessity for each is properly evaluated. It should be emphasized again that mercurial diuretics do not take the place of digitalis in the treatment of congestive heart failure.

ROUTES OF ADMINISTRATION

Preparations of the mercurial diuretics are available for intravenous, intramuscular, and subcutaneous use as well as for oral and for rectal administration

Until recently the administration of mercurial diuretics intravenously appeared to be best suited to general use *Thiomerin,** a mercurial diuretic recently devised for subcutaneous use, provides a drug which has wide application in treating congestive heart failure The mercurial diuretics were given routinely by intravenous route in the Cardiac Clinic of the New York Hospital until the introduction of the subcutaneous preparation Increasing numbers are now being given thiomerin subcutaneously.

* Wyeth, Inc

Intravenous Route

Intravenous injections are more comfortable for patients than intramuscular ones and, with care, veins can be used for years without damage to them.

Technic

A 26-gauge hypodermic needle is used for intravenous injections. The needle should be sharp, care should be taken to see that the point does not have a barb on it. With such a needle the smallest veins, such as those on the back of the hand, may be entered successfully.

The injection should be made slowly. Two to three minutes should be required to inject 2 cc, each drop being followed by a pause. There is no need for dilution with salt solution. On withdrawal of the needle the arm should be held straight up with pressure over the site for a few minutes to avoid extravasation of blood (The common practice of putting a sponge in the antecubital space and bending the elbow tightly acts as a tourniquet and frequently causes a small hematoma) With ambulatory patients in the clinic or office we make the patient wait 15 to 20 minutes after the injection before going home. Reactions have not been observed in our clinic from the use of these drugs intravenously in a large case load of patients over many years.

Preparations

Mercuzanthin, *salyrgan-theophylline*, *mercuhydrin*, and *thiomerin* are available for intravenous use. Mercuzanthin and salyrgan-theophylline have been used more extensively than the other preparations by this route. In mercurophylline (formerly mercupurin but now known as mercuzanthin) the theophylline and the mercury compound are in approximately molar proportions. In mersalyl and theophylline (sold as salyrgan-theophylline) and meralluride sodium solution (mercuhydrin) the theophylline is in excess.

Dosage

If there is no urgency and the patient has not been given a mercurial diuretic previously, 1 cc. of the preparation can be given intravenously as a trial dose. Idiosyncrasy is, however, rare, and frequently 2 cc. is given on the first injection. In certain instances the smaller dose induces an adequate diuretic response and larger amounts are not required, although 2 cc. may be given in later injections. The 2-cc injection usually results in excellent diuresis amounting to 2000 cc. or more in 24 hours on a 1200 cc. fluid intake (Fig. 2). We rarely use more than 2 cc. and this dosage is now common practice.

Intramuscular Route

The injection is usually made deep in a gluteal muscle with a 22-gauge needle. The plunger should be drawn back to be certain a vein is not entered before the injection is made. Many patients complain of discomfort and soreness in the injection area for some while afterward. It is claimed that this route is safer than the intravenous route since most of the fatalities have occurred after intra-

venous injections (see p. 46). Provided safety factors are equal when the drugs are given by these two routes of administration, the time that can be saved in giving the intravenous preparation, as compared with that required for intramuscular injections, is enormous when 50 to 70 injections are to be given at a clinic session.

Preparations

Mercuzanthin, salyrgan-theophylline, mercuhydrin, thiomerin and *mercuprocyl* are available for intramuscular use. The intramuscular dose of these drugs is the same as the intravenous dose.

Subcutaneous Route

Thiomerin, as already mentioned, can be given not only intravenously and intramuscularly but also subcutaneously. Stewart, McCoy, Shepard, and Luckey found

1. that this mercurial preparation is an effective diuretic when given subcutaneously (Fig. 3),
2. that it was as potent a diuretic agent, when comparison was possible, as the other mercurial diuretics,
3. that in many instances it was more effective as a diuretic than the other mercurial preparations,
4. that there was only transient discomfort, such as burning at the site of injection,
5. that subcutaneous nodules which occurred at the site of injection in a few patients when the earlier preparations of this drug were available are rarely encountered in the latest batches of this drug,
6. that no significant toxic effects have so far been encountered from the drug as we have used it,
7. that it is possible to keep patients in a state of compensation, free of fluid accumulations, on this preparation just as easily as with the other mercurial diuretics;
8. that in certain patients it was possible to reduce the number of injections or the dose compared with the other mercurial diuretics;
9. that the diuresis following a subcutaneous injection occurred over a longer period of time, running over into the second 24 hours, as compared with the other preparations. Patients volunteered the observation that because the diuresis was less drastic but more prolonged they were less fatigued and less weak after thiomerin diuresis;
10. that most patients have come to prefer this drug given subcutaneously to other mercurial diuretics by the intravenous and intramuscular route.

Dosage

In our clinic we are using the subcutaneous route for most patients. Unless there is urgency we usually prescribe 0.5 to 1.0 cc. as a trial. In some patients 1.0 cc. once or twice a week, or every third day, is adequate; in others, in whom adequate diuresis does not result, 2.0 cc. may be required. We have not used and do not recommend amounts greater than this, nor that the interval between injections

be shorter than two days, although in a few instances the drug has been given every other day and in fewer instances daily without apparent toxic effects.

Care should be exercised that the drug be given *subcutaneously* and *not intradermally. A small area of sloughing of the skin occurred in one patient in whom* the injection was made superficially into the skin. Injection can be made in the subcutaneous tissues of the arm or of the thigh. It is best not to inject the drug into edematous tissues, lest its absorption be interfered with or delayed.

Our experience with thiomerin is similar to that reported by other clinics.

Self-administration

Krehbiel and Stewart have observed a group of patients who have been taught to administer thiomerin to themselves subcutaneously By demonstration and then by practice, patients are taught the sterilization of needles and syringes and the technic of drawing the proper amount of the drug from the sterile bottle of thiomerin without contamination. Then they are taught how to inject the drug subcutaneously in themselves and how to maintain a sterile technic. After we are satisfied that patients are competent to carry on alone with their injections they give the drug to themselves once or twice a week as ordered by their physicians and report for examination every two to four weeks. Certain patients are trained to make up the thiomerin solution

PRACTICAL ADVANTAGES OF SELF-ADMINISTRATION. There was precedent for the self-administration of this drug in the experience of patients being taught to give insulin. The economic importance of patients requiring frequent and regular mercurial injections being able to give themselves a certain number of these injections is apparent: It spares the patient the extra effort and loss of working time in going to the physician or clinic, and it decreases the case load for clinics and doctors of patients who come only for mercurial injections. At the present time only patients who are in water equilibrium, and who are on regular mercurial regimens, and those in whom the patterns of response to mercurial diuretics are known, are being trained in self-administration of this drug. Patients are given advice to come to the clinic or physician at once should the drug fail to induce diuresis, should they have untoward symptoms, and should they not continue to feel well. The drug has been supplied only to those patients whose reliability and cooperativeness has been well established

Thiomerin Preparation

When it is made up in solution thiomerin has a limited period of stability For this reason it is supplied as a powder in a sterile container with a rubber cap together with an ampul containing the appropriate amount of sterile distilled water. The drug is supplied in two amounts so that it can be made up in 10 cc and 30 cc. quantities. The batches of the drug *which are now available remain* stable after being made up into solution for a period of several months at room or icebox temperature. The 10 cc. amount is therefore convenient for patients getting injections once or twice a week. The solution should not be used if it becomes turbid or if black particles precipitate out. Not all patients can be trained in the sterile technic of making up the solution, even though they may be capable of giving their own injections.

Plan for Injections

Frequency of Injections

In both ambulatory and bed patients when the need for a mercurial diuretic arises the frequency and duration of the injections are determined by the circumstances under which heart failure occurs and by their effectiveness.

The drug may be given every third day, if adequate diuresis is obtained. When given to bed patients it is usually wise to maintain this schedule, provided untoward results do not occur, until the patient is mobilized and his functional capacity is assayed. After the patient is mobilized it may be safe to increase the interval between injections gradually to arrive at one which will keep the patient free of congestive heart failure, with the recurrence of only a few râles at the lung bases. The interval between injections may be increased to once a week or longer if a favorable response continues A slight gain in weight as the urine output decreases is allowable, provided that the weight does not rise to the height preceding the injections. The frequency of injections for ambulatory patients is adapted to their requirements to maintain compensation

I do not like to give mercurial diuretics oftener than every third day Nor do I subscribe to the daily injection of small amounts such as 0.5 to 1 cc. because it causes needless injections and the small increments in urine output from this amount do not equal in proportion the output from a larger injection. Emphasis is placed on this since daily injections have been recommended as a means of dehydrating patients The so-called "dehydrating regimen" is not recommended. It is discussed further on page 48.

Duration of Requirement for Mercurial Diuretics

The duration of use of the mercurial diuretics may vary considerably. In pulmonary edema one injection may be adequate. After an episode of congestive heart failure precipitated by a unique series of events the drug may be required only until restoration of compensation. In the greatest number of cardiac patients who have congestive manifestations, however, prolonged use of the mercurial diuretics is necessary in order to restore compensation, and then to maintain it Injections may be required as often as two to three times a week at first. After the fluid accumulations have disappeared with satisfactory diuresis the interval between injections may be lengthened. The objective should be to keep the patient free of congestive manifestations. Frequently in ambulatory patients the nearest approach to this objective is the following: a slight gain in weight, a few basal râles, and recurrence of minimal edema by the time of the next injection Dehydration should not occur. Great numbers of patients have been given mercurial diuretics over many years without harm. Nevertheless it is wise to have occasional routine urine examinations and blood urea nitrogen estimations to detect renal damage.

Time of Day

While patients are in the hospital mercurial injections, except in an emergency, should be given in the morning so that diuresis occurs before night and does not interfere with sleeping. Injections should be given as early as possible to ambulatory patients.

Digitalis Intoxication

I have not seen digitalis intoxication occur when digitalized patients with ascites are given mercurial diuretics. There has been ample occasion for this manifestation to be detected if it had occurred The action of mercurial diuresis in mobilizing digitalis which may be present in ascitic fluid seems to be only of hypothetical interest. If the serum potassium is lowered the heart muscle may be more sensitive to the concentration of digitalis

Oral Route

There has been some experience with the oral use of mercurial diuretics. They are given as enteric coated tablets. *Mercuzanthin* and *salyrgan-theophylline* are available The oral dosage has not been as accurately defined as the dosage by the parenteral routes. Gastric irritation may be avoided by giving the tablets after meals. Patients may have nausea and vomiting and gingivitis. The diuretic effect when the mercurial drugs are given orally is slower and lasts longer than when the drug is given by injection. Some physicians recommend a combination of the oral and parenteral routes in order to avoid too frequent injections.

Dosage

The drug is best given in divided doses Each *mercuzanthin* tablet* for oral use contains a concentrate of mercurophylline injection (U S P.), namely 120 mg of mercuzanthin, which is equivalent to 30 mg. of mercury and 27 mg. of anhydrous theophylline. Five tablets given at one time are said to induce a diuretic response comparable to that of 2 cc of mercuzanthin given intravenously While one or two tablets a day may be adequate in mild edema, one to three tablets three times a day may be required to produce an adequate diuresis An interval of two or three days should elapse before the oral medication is repeated

Each tablet of *salyrgan-theophylline* (mersalyl theophylline)† for oral use is equivalent to 80 mg of salyrgan and 40 mg. of theophylline The mercury in the salyrgan amounts to 31 7 mg.

Derow and Wolff think that the oral administration of mercurial diuretics (mercuzanthin) is a valuable adjunct to the treatment of congestive heart failure For certain patients they found its use by this route more practical and more effective than by the intravenous route They were of the opinion that minor toxic effects, such as abdominal cramps with or without diarrhea, bloody stools, and gingivitis, need not be contraindications if the patient is followed carefully. Patients should be seen once a week They recommend that the schedule be suited to the patient and offer four plans:

1. the daily schedule which provides for three tablets every day in the morning before breakfast or one tablet three times a day,
2. the five-days-a-week schedule, in which one tablet is given three times a day or two tablets every morning before breakfast;
3. the every-second-day schedule, with three tablets given in the morning,

* Campbell Pharmaceutical Co
† Winthrop Stearns.

4. a variation of the every-second-day schedule, with two to three tablets given in the evening.

One patient in their series died of renal insufficiency with hypochloremia, hypoproteinemia, hypercholesterolemia, anasarca, and shock. The urine showed four plus albumin.

I do not recommend the use of mercurial diuretics orally. It is not a safe procedure to allow patients to have tablets of these drugs because they may be inclined to "treat themselves" instead of going to the physician, and to take increasing amounts of the drug of their own volition when the usual amounts are ineffectual. Slow accumulation of mercury with toxic effects may result. The oral medication has not found wide application.

Mercurial Suppositories

Suppositories of *mercuzan* and *salyrgan-theophylline* are available. They give rise to diuresis in a large number of patients but their effectiveness cannot be relied upon. Mer [illegible] nt to about 0 2 ([illegible] times the quanti [illegible] mercurial diuretic Suppositories should be used only after a careful rectal examination has established the absence of hemorrhoids. They frequently cause rectal irritation. The suppository should be given one to two hours after a cleansing enema. It should not be used oftener than every two or three days Since satisfactory mercurial preparations are available for intravenous, intramuscular, and subcutaneous use, it is only on rare occasions that suppositories may be required

AMMONIUM CHLORIDE TO ENHANCE THE DIURETIC EFFECT

In certain instances mercurial diuresis appears to be enhanced by the administration of ammonium chloride (Fig 2). The use of this drug has been discussed in Chapter 1, p. 16.

AMINOPHYLLIN TO ENHANCE THE DIURETIC EFFECT

Vogl and Esserman have found that the simultaneous intravenous injection of aminophyllin and one of the mercurial diuretics and the continued administration (intravenous or intramuscular) of aminophyllin on the days the mercurial drug is not given enhance the diuretic effect of the mercurial and also maintain continuous diuresis. For example, on the first day, aminophyllin 0.5 Gm is given with 2.0 cc. of the mercurial diuretic in the same syringe intravenously in the morning. Aminophyllin is repeated intravenously or intramuscularly in the evening, and is given in the same amounts twice a day on the second and third days This three-day schedule can then be repeated as indicated. They recommend this schedule for patients with advanced heart failure who are refractory to mercurial diuretics.

* Campbell Pharmaceutical Co

BENEFITS DERIVED FROM MERCURIAL DIURETICS

In most patients, especially on the first exhibition of *mercurial diuretics*, satisfactory diuresis results In some instances the 24-hour urine output may increase to as much as 4000 to 5000 cc. with a corresponding loss in body weight with each injection, when the fluid intake is 1200 to 1500 cc. (Fig. 2). The urine output is commonly around 2000 cc. or more in the early stages when ample fluid accumulations are available for excretion as urine. It is rare in early heart failure, or on the first exhibition of these drugs, that diuresis fails to occur. In the interval before the next injection the urine output decreases and the patient gains weight. With the next injection there is further diuresis with loss of weight to new lower levels. With adequate diuresis at this stage in therapy the weight does not return to the level preceding injection (Fig 2). There is accordingly a progressive fall in weight with gradual lessening of the signs and symptoms of heart failure until compensation is restored.

Emphasis has already been placed on the method of giving the drug with a two-day free interval between injections so that there is opportunity for the serum electrolytes and body water to strike a new balance and to make appropriate adjustments Patients do not have their rest disturbed by continuous diuresis, and the fatigue and weakness which accompany prolonged diuresis need not occur. As the stored fluid becomes less and patients attain stabilization at their lowest weight, the response to the mercurial drug decreases, depending on how much fluid is stored in the body after the last injection

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PREPARATIONS OF MERCURIAL DIURETICS

Preparations of Campbell Pharmaceutical Co.

Mercuzanthin (Mercurophylline U S.P. XIV) is sodium trimethyl-cyclopentane-dicarbonic acid-methoxy-mercury-allylamide-theophylline It is suitable for intravenous or intramuscular use. Each cubic centimeter contains 100 mg. of the mercury compound, equivalent to 39 mg. mercury and 36 mg. of anhydrous theophylline

Mercuzanthin tablets are available for oral use Each tablet contains a concentrate of U.S P. mercurophylline containing 120 mg. mercuzanthin which is equivalent to 30 mg of mercury and 27 mg of anhydrous theophylline

Mercuzan suppositories· "Mercuzan is a complex synthetic mercurial containing about 40 per cent of mercury prepared from d-camphoric acid and a racemic substituted propylamine. It is a mixture of 20 per cent of the beta-methoxy-gamma-hydroxy-mercuripropylamide of trimethyl cyclopentane dicarboxylic acid and 80 per cent of its sodium salt."* Each suppository contains 0.5 Gm of this compound amounting to approximately 0.2 Gm. mercury. In short, it contains two and one-half times the amount of mercury present in 2 cc. of mercuzanthin for parenteral use.

* From the Campbell Pharmaceutical Co brochure.

PREPARATION OF WYETH INCORPORATED

Thiomerin (Mercaptomerin N.N.R.) is the disodium salt of N(gamma-carboxymethylmercaptomercuri-beta-methoxy) propyl camphoramic acid and has the following structure:



One cubic centimeter of thiomerin contains 40 mg mercury This drug can be used intravenously and intramuscularly. It gives rise to excellent diuresis. More important however is the fact that it can be given subcutaneously. The manufacturers, recognizing the advantages of a potent mercurial diuretic suitable for subcutaneous use, are stressing this route of administration

PREPARATIONS OF WINTHROP-STEARNS

Salyrgan-theophylline (mersalyl with theophylline U.S.P. XIV) is suitable for intravenous and intramuscular use One cubic centimeter contains 0.1 Gm. salyrgan (equivalent to 39 6 mg. mercury) and 0 05 Gm. theophylline.

Salyrgan-theophylline is also available for *oral* use. Each tablet contains 80 mg. salyrgan and 40 mg. theophylline. This amount of salyrgan has 31.7 mg. of mercury.

Salyrgan-theophylline is also available as a *suppository* for rectal use

PREPARATIONS OF LAKESIDE LABORATORIES

Mercuhydrin (Meralluride N N R.) is the sodium salt of methoxoxi-mercuri-propyl-succinyl-urea with theophylline. Each cubic centimeter contains 39 mg mercury in organic combination together with 48 mg. theophylline It can be used both intravenously and intramuscularly but the manufacturers advise the latter route.

PREPARATION OF PHARMACEUTICAL ORGANICS

Mercuprocyl is salyrgan-theophylline to which procaine is added in order to decrease the discomfort of intramuscular injection. It is for intramuscular use only

TOXIC MANIFESTATIONS

Mercurial diuretics should be used with care and in appropriate circumstances. There should be clear-cut indications for their use. During prolonged use the urine should be examined at intervals to detect the presence of albumin, red blood cells, and casts. With any change in the patient's response to the drug, with the occurrence of nausea or vomiting, or when diuresis fails to occur, urinalyses and estimations of the blood urea nitrogen should be carried out. These diuretics should not be used in patients with marked reduction in renal function.

The use of mercurial diuretics in the treatment of obesity, to induce dehydration to lower the blood pressure, and as a part of the regimen of treating angina in the absence of heart failure should be discouraged. Mercurial diuretics should not be used in acute or chronic nephritis We have used the drug effectively at times in the nephrotic type of glomerulonephritis, but only when other means of mobilizing fluid were ineffective.

Modifications to Prevent Toxicity

Because of the reported sudden deaths after intravenous injections, attention has been focused on the intramuscular route. Thiomerin, mercuzanthin, salyrgan-theophylline, and mercuhydrin can be given intramuscularly but because many patients complain of pain of varying degree at the site of the injection, procaine has been added to salyrgan-theophylline. It is distributed under the name of mercuprocyl.* A few patients are sensitive to procaine, and because of the extensive use of mercurial diuretics this does not appear to be the best solution to the problem. Thiomerin, which has been devised as a mercurial diuretic for subcutaneous as well as intravenous and intramuscular use, has certain advantages which may solve some of these problems.

In passing, the antagonistic effect of morphine and demerol on mercurial diuresis in certain patients is mentioned.

Forms of Toxicity

Sudden Death

The few instances of sudden death after intravenous injection have been due to ventricular asystole or ventricular fibrillation Transient ventricular rhythms have also been recorded in patients following the intravenous route of injection. Accidents have indeed been few in relation to the enormous quantities of these drugs which are used This, however, is not adequate reason for not finding the situations in which the drugs are contraindicated or for seeking less toxic preparations. No doubt some of the reactions and deaths could have been prevented by insisting that every injection of the drug be made very slowly. When this is done there is ample opportunity to question the patient about symptoms and to observe the appearance of signs of distress and of change in respiratory pattern It is then possible to stop the injection in time to prevent more serious manifestations

Some physicians think that these drugs should only be given intramuscularly. This route has the advantage that it can be used by the nurse without supervision. When prompt and assured absorption is the objective, the intravenous route is preferred. The incidence of ventricular paroxysmal tachycardia and ventricular fibrillation should be diminished by the use of thiomerin.

Precordial Distress

On rare occasions patients complain of slight tightness in the chest during the intravenous injection of mercurial drugs. This may be associated with the theophylline radical. When it is necessary to use mercurial diuretics in patients who have experienced this symptom the intramuscular route may be substituted or the intravenous injection slowed still further Thiomerin which can be given subcutaneously is also available for such patients.

Gastrointestinal Symptoms

Occasionally nausea and vomiting occur several hours after intramuscular or intravenous injection. Very rarely patients complain of slight nausea at the height of

* Pharmaceutical Organics

diuresis Resting after the injection may prevent these symptoms, and they may not occur if a different mercurial preparation is employed. Nausea and vomiting *without diuresis* is an indication for discontinuance of the drug.

Rarely nausea and vomiting occur *during* intravenous injection. In some of these patients we have given 2 cc. of saline intravenously with a similar reaction, and have

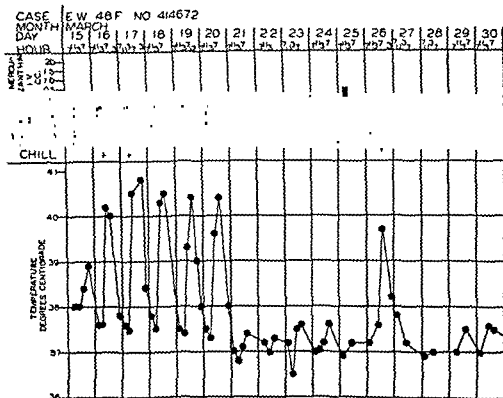


Fig 4

Data Relating to a 48-Year-Old Woman with Heart Failure and Febrile Reaction to Mercuhydrin With each intramuscular injection of 2 0 cc mercuhydrin temperature rose to as high as 40.8° C. (on two occasions with chills), and promptly fell to normal (March 15 to 20 inclusive) On the days mercuhydrin was not given, patient did not have fever (March 21 to 24 inclusive) On March 25 0 5 cc of mercuzanthin was given intravenously, and rise in temperature did not occur [illegible]

concluded that it was due to an emotional factor Diarrhea is rarely encountered *from the preparations which are now available*

Fever

Rises in temperature to as much as 40° C. may follow either the intravenous or the intramuscular *injection of the drug (Fig. 4). When a febrile reaction* occurs with one mercurial diuretic another of these drugs can usually be substituted to

eliminate this reaction. The days on which the injections are given should be indicated on the temperature chart in order to discover whether a coincidence exists between them and the temperature rises. I have not yet observed febrile reaction following thiomerin.

Cramps in the Calves of the Legs—Salt Depletion

During the height of mercurial diuresis patients may complain of pain in the calf muscles of the legs. This is usually due to the loss of sodium chloride. Patients who have been on a low salt intake for a long time experience this symptom most frequently. The mechanism is similar to that of heat cramps of stokers or during severe sweating in summer. The cramps are promptly relieved if the patient takes a little table salt by mouth. One or two Saltine crackers or a small amount of dried chipped beef will supply this without danger of overdosage. Patients should be told about the mechanism of the cramps. It is emphasized to them that salt in this situation is used as a medicine. Its temporary need at that particular time does not mitigate the necessity for the maintenance of the rigid salt-poor diet. The occurrence of cramps in the legs does not require discontinuance of mercurial therapy. Cramps due to loss of calcium are described on the opposite page.

Dehydration

When mercurial diuretics are given by the intramuscular, intravenous, or subcutaneous route every third day or at most every second day, dehydration does not usually occur. During therapy signs of heart failure and the response of the patient to the drug must be carefully observed as these are used as guides to the frequency of injection and to the dosage.

Dehydration is a pathologic state, indicating a serious disturbance of water and salt metabolism, and is not a desirable therapeutic objective. I have warned against the daily administration of a mercurial diuretic because patients may develop a state comparable to shock from the loss of sodium chloride during continuous, vigorous diuresis. The blood may become so dehydrated that its increased viscosity puts a heavier load on the heart and may promote intravascular clotting since the velocity of blood flow is slow in heart failure. It is recalled that thromboembolic phenomena frequently occur in heart failure. In patients with the high specific gravity of the blood of polycythemia, together with congestive heart failure, diuresis may give rise to thrombosis and cerebral accidents may result.

Continuous diuresis may result in disproportionate loss of chloride in relation to sodium in the urine, in a rise in the carbon dioxide combining power of the blood, and in a fall in serum chloride.

Weakness from Potassium Depletion

Patients who are on a low salt diet may complain of extreme weakness after profuse mercurial diuresis. This symptom may be due in part to the loss of sodium chloride or to a change in intracellular electrolyte balance in an attempt to compensate for the salt depletion. Or it may be due in part to loss of potassium. Mercurial diuretics do not usually result in the increased excretion of potassium. If the food intake is adequate hypopotassemia will not occur. On the other hand if the patient

fails to eat, and potassium is not provided, the kidneys do not conserve potassium but continue to excrete it and hypopotassemia results. Weakness due to potassium depletion is coming to be recognized more frequently. When this is the case the restoration of potassium should be carried out very carefully, as patients with heart failure may not be able to excrete the added amounts. When potassium loss results from diuresis, its replacement either by Locke's or Ringer's solution has not, in my experience, been required. It might be advised if excessive diuresis has given rise to a state of shock.

Tetany and Calcium Depletion

Tetany has been reported following marked mercurial diuresis. It is due to loss of calcium in the urine. Patients complain of cramps and may have carpopedal spasm and laryngospasm The Q-T interval in the electrocardiogram is prolonged. The blood calcium is found to be low The intravenous injection of 10 cc. of a 10 per cent (0.08 Gm.) solution of calcium gluconate is indicated If the pattern is repeated the daily use of milk and of calcium orally may prevent its occurrence. In a long experience with mercurial diuretics I have not seen tetany occur.

Skin Rash

Skin rashes due to mercurial diuretics have been reported. I have not had occasion to see this reaction (see Sensitization, below). The preparation causing the reaction should be discontinued, and another substituted. It is possible that pyribenzamine might give relief from this symptom.

Mercury Poisoning

We have many patients who have been on one or another of the mercurials for many years without the occurrence of mercury poisoning Instances of gingivitis and loosening of the teeth have been reported With the appearance of these signs, the mercurial drug should be discontinued. All patients receiving these diuretics should maintain good oral hygiene

Toxic Nephrosis

Toxic nephrosis has been described from the continued use of mercurial diuretics. Mercury has been found in the kidneys and liver at autopsy. When anuria occurs it may not be possible to combat it successfully It is treated as are other cases of anuria, such as that resulting from transfusion Bilateral decapsulation of the kidneys or sympathectomy may be tried Large amounts of fluids may be given intravenously. The use of BAL might be considered when early changes in renal function or appearance of cellular elements or albumin in the urine point to kidney damage I have not seen instances of such damage

Sensitization to Mercurial Diuretics

I have observed one instance of sensitization to a mercurial diuretic. A patient who had received salyrgan intravenously twice a week for many years developed a skin rash of the exfoliative dermatitis type. A consulting dermatologist did not think at first that it was due to the mercurial diuretic because such an instance had

not been reported previously, and the salyrgan was continued. When the rash became worse the drug was stopped. The patient improved promptly and recovered. Later a patch test showed sensitivity to salyrgan, and use of the drug was permanently discontinued Mercuzanthin was later used for many years in this patient without any evidence of sensitivity.

Neutropenia

Bender, Hoxsey, and DeMarsh have recently reported an instance of neutropenia in a patient treated with a mercurial diuretic (mercupurin). This blood dyscrasia responded favorably to the use of BAL.

SUMMARY

The mercurial diuretics have come to be almost indispensable in the treatment of patients with congestive heart failure. The response to this form of therapy may be dramatic and long lasting As valuable as they are in the treatment of congestive heart failure, it should be emphasized that these drugs supplement rather than supplant digitalis in the treatment of congestive heart failure Drug manufacturers have done a good job in the continued search for better drugs of this series of diuretics and progress continues It is a source of satisfaction that drugs as potent as the mercurial diuretics can be given under such varying circumstances, and in almost fantastic numbers of injections, without more frequent occurrence of toxicity. To make sure that these valuable drugs are wisely used, one should keep in mind (1) establishment of need for the use of the mercurial drug, (2) consideration of the safety of its use, (3) the exercise of meticulous care in the giving of the drug, and finally (4) foresight that the drug is not given too frequently.

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CHAPTER 3

Digitalis

INTRODUCTION

Digitalis is our most effective drug for the treatment of congestive heart failure and of certain abnormal rhythms of the heart Its place in the treatment of patients with heart disease has remained unchallenged since Withering first advocated its adoption for the treatment of dropsy in 1785 No other drug has been the subject of greater interest or of more extensive investigation Although other drugs have been discovered which contribute to the treatment of heart failure and the abnormal rhythms a substitute for digitalis has not been devised

The exact mechanism by which digitalis induces its beneficial effects is still the subject of study Certain of these effects can be observed by every physician, but they are capable of several interpretations when attempts are made to fit them together into a unified concept. Physicians should be acquainted with those effects of the drug that can be recorded or expected from its use under ordinary circumstances They should be aware of both its therapeutic and its toxic effects, although the aim should be—and its attainment is possible under most conditions—to achieve therapeutic effects without toxicity

GENERAL SURVEY OF DIGITALIS PREPARATIONS

Infusions of the digitalis leaves were the first form of the drug, and were followed by the tincture and eventually the whole leaf Attempts to isolate the active principles of digitalis have been increasingly successful As a result, purified drugs rather than a mixture of the digitalis bodies are available for use The infusion and the tincture are now rarely employed.

Whole Leaf

Tablets of the whole leaf are satisfactory for the routine digitalization and maintenance of most patients These aims can be accomplished effectively and rapidly if the digitalizing amount of the particular preparation has been established for patients beforehand (see below).

Glycosides

Certain purified glycosides of digitalis have therapeutic effects which parallel those of the whole leaf and therefore can be substituted for it when occasion requires. These preparations have different rates of absorption and of excretion or dissipation, which must be known before the drugs are used clinically, and each of them has a different margin of safety between the therapeutic and the toxic amounts.

Although the digitalizing amount of each glycoside must be established, once it has been established it remains fixed since the glycosides are chemical entities On the other hand the digitalis leaf varies not only according to the place where the leaves are grown but also according to the crop from year to year. Accordingly, each separate preparation of the whole powdered leaf requires standardization on patients.

There are, however, factors which make the whole leaf a better preparation for routine use. For instance, as we shall see later, maintenance of a patient in digitalis equilibrium may be more difficult when one of the glycosides is used because these substances are excreted either more rapidly or more slowly than is the whole leaf.

ESTABLISHMENT OF DIGITALIZING AND MAINTENANCE DOSES

Standardization of digitalis by the pigeon method (U S.P.XIV) aims to supply digitalis of uniform potency. The amount of the preparation required to induce certain effects in patients must, however, also be established.

Experience has shown that the clinical strength of a digitalis preparation can be determined by observing its effect in slowing the ventricular rate to around 70 beats per minute in the presence of auricular fibrillation with a rapid ventricular rate. The amount required to achieve this rate is the optimal therapeutic amount when it is given within 24 hours. While it is obvious that some measure of benefit accrues from smaller amounts while the ventricular rate is slowing, such amounts do not yield maximal benefits and are therefore not optimal. On the other hand, it has been demonstrated that, with one exception, greater benefit does not result from the administration of amounts of these drugs which induce toxic signs such as nausea and vomiting. The exception occurs when it may be necessary to induce minor toxic effects before digitalization will terminate auricular flutter or attacks of [illegible] It is also worth noting that the digitalizing amount [illegible] ricular fibrillation can be [illegible] in other instances when digitalization is indicated.

The digitalizing and maintenance amounts of whole digitalis leaf and digitoxin have been rather precisely defined, but have not been so accurately established for the other glycosides.

Whole Leaf

Digitalizing Dose

Observations on three or four patients may be required to establish the clinical strength and average digitalizing amount of a preparation (Figs. 5 and 6).

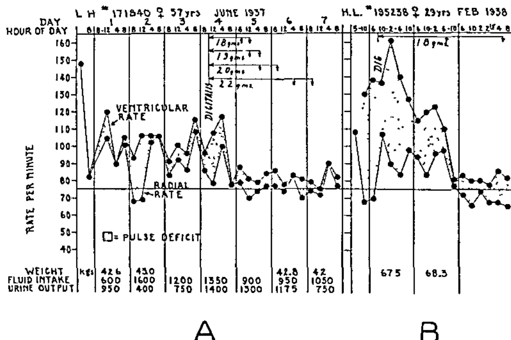


Fig 5

Effect of Digitalis Leaf on Ventricular Rate and Pulse Deficit in Two Patients With Auricular Fibrillation In this and the following charts, the upper series of dots represent the apical heart rate, the lower series of dots, the radial rate, the stippled area, the pulse deficit, and a vertical bar shows the time digitalis was first given Amounts along vertical line indicate total amount of digitalis preparation which patient received from the beginning to the end of the horizontal line with an arrow at the end Times at which additional amounts of drug were given are indicated by arrows downward from the horizontal line Total amount of digitalis up to any one day, its distribution, and its effects are apparent.

A A woman 57 years of age 1 8 Gm of the whole leaf preparation (New York Heart Association) in 24 hours was adequate to slow the ventricular rate and 0 1 to 0 2 Gm for maintenance

B A woman 29 years of age 1 8 Gm of the whole leaf in 24 hours was adequate to slow the ventricular rate No evidences of toxicity Digitalizing amount of this preparation was 1 8 Gm

The patient with auricular fibrillation and a rapid ventricular rate, who has had no digitalis for three weeks, is put to rest in bed for a few days—until the pulse deficit chart shows that the ventricular rate is stabilized or has increased. Digitalis is begun in the morning The objective is to give enough of the drug in 24 hours to slow the ventricular rate to approximately 70 beats per minute. In this case

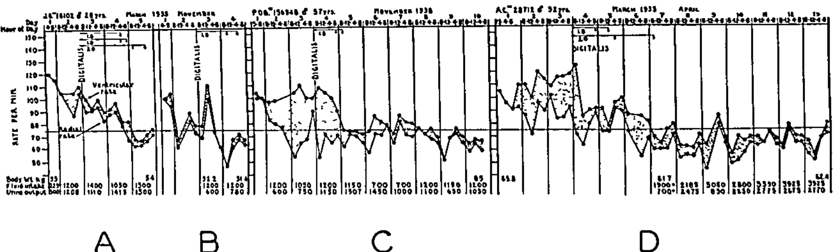


Fig 6

Effect of *Digitalis Leaf* (*New York Heart Association Preparation*) on *Three Patients with a Range in Weight from* 51 Kg to 85 Kg. In each patient 1.8 Gm was adequate to slow the ventricular rate. A and B relate to two admissions of the same patient

excretion may be neglected. Apical and radial rates are counted frequently during digitalization. If the approximate potency of the preparation is known, about one-half that amount can be given by mouth at once, to be followed by decreasing amounts every few hours, the fall in ventricular rate being the guide. In the first patient of the series, while trying to obtain a rough impression of the strength of the preparation it is best to stop short of the therapeutic amount, in order not to induce toxicity. Should the therapeutic amount be inadvertently exceeded, a smaller

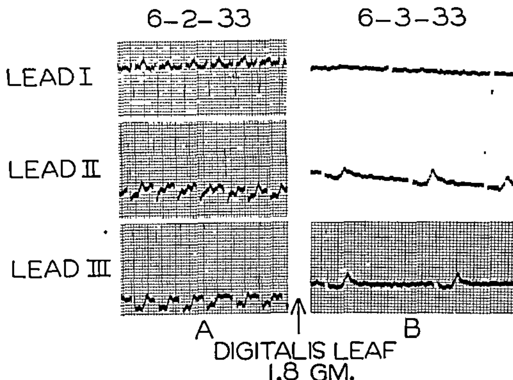


Fig 7.

Effect of Digitalis in a Woman 32 Years of Age with Rheumatic Heart Disease and Auricular Fibrillation A
the oral adminis
digitalization, 60

amount is given to the next patient Experience with the digitalis leaf prepared for the New York Heart Association (U.S.P XIV) has shown that 1.8 Gm *is the average digitalizing amount* (Figs. 5 and 7).

lation to body weight and
except in infants (Figs 5
rapid auricular fibrillation
whom I have observed, approximately the same amounts of the drugs were required to slow the ventricular rate to 70 beats per minute as was necessary for adults I have had no experience with children under three and one half years of age. (Dosage of digitalis for children is discussed further on page 97.)

Maintenance Dose

When the ventricular rate has been reduced to a resting rate of between 60 and 70 beats per minute it is maintained at the lower level by daily ration amounts of the drug, administered with the patient remaining in bed. Adjustment of the dose

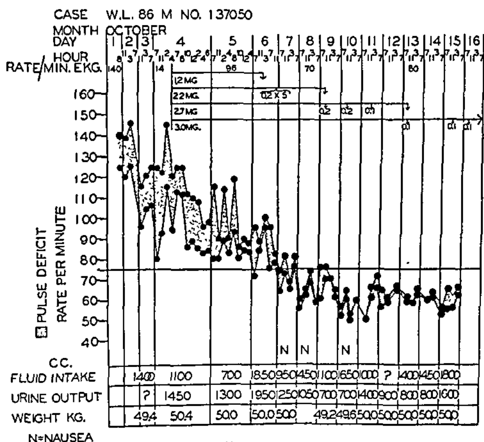


Fig. 8

required to maintain the rate is accomplished by analysis of the preceding day's pulse deficit chart. The total maintenance amount after digitalization, divided by the number of days of observation (excluding the day of digitalization), represents the average daily ration amount.

The ration dose varies from patient to patient but the average maintenance of the whole leaf is 0.2 Gm. daily.

Digitoxin

The digitalizing and maintenance amounts of the glycosides are established in the same manner for patients with auricular fibrillation as has been described for the whole leaf. With respect to digitoxin it has been found that 1.2 mg. given

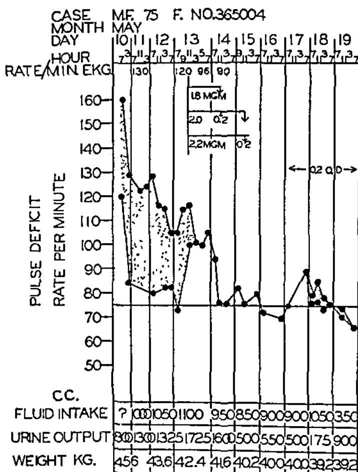


Fig. 9

Effect of Digitoxin in a Woman 75 Years of Age with Auricular Fibrillation. Initial dose of 1.8 mg. was adequate to slow [illegible]
0.2 mg. daily are shown. No [illegible]
was 1.8 to 2.0 mg. (Stewart, [illegible]
nativelle) required f[illegible] 1940.)

orally in one dose is inadequate to slow the ventricular rate (Fig. 8), additional amounts are required to complete digitalization. In most instances 1.8 to 2.0 mg. slows the rate if given in one dose or in broken doses over a 24-hour period (Fig. 9) and is the *average digitalizing amount*. In those patients in whom more than this is required the additional amounts bear no relationship to the body weight. For

Maintenance Dose

When the ventricular rate has been reduced to a resting rate of between 60 and 70 beats per minute it is maintained at the lower level by daily ration amounts of the drug, administered with the patient remaining in bed. Adjustment of the dose

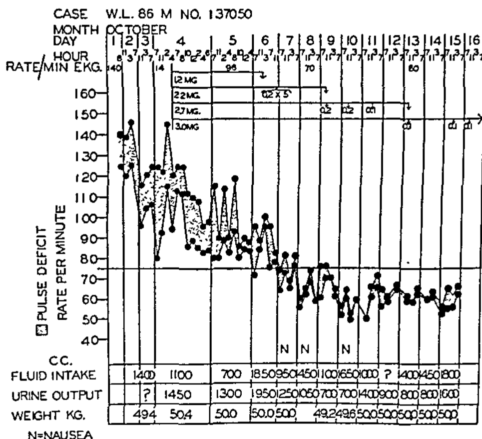


Fig 8.

required to maintain the rate is accomplished by analysis of the preceding day's pulse deficit chart. *The total maintenance amount after digitalization, divided by the number of days of observation (excluding the day of digitalization), represents the average daily ration amount.*

The ration dose varies from patient to patient but the average maintenance of the whole leaf is 0.2 Gm. daily.

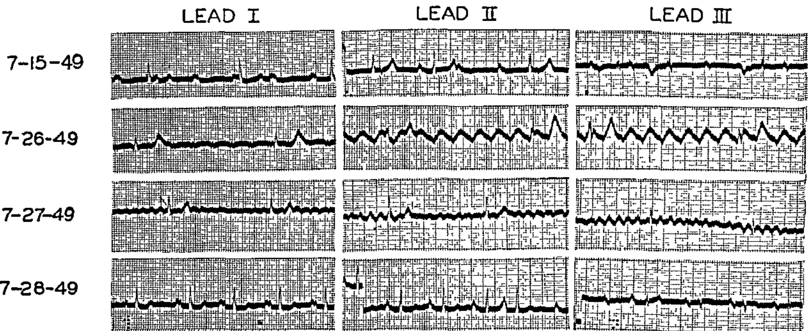


Fig. 11.

Certain Toxic Effects of Digitoxin in a Woman 45 Years of Age Patient was on maintenance doses of digitoxin. Electrocardiogram taken July 15, 1949 showed complete heart block, auricular rate being 88 and ventricular rate 37 Digitoxin was discontinued and within a few days complete heart block disappeared and digitoxin was again started In electrocardiogram taken on July 26 auricular flutter was present with complete heart block. Auricular rate was 187, ventricular rate 25 Digitoxin again discontinued On July 27 auricular fibrillation with runs of impure flutter with complete heart block was present. Ventricular sequence was regular, the rate being 34 On July 28 normal sinus rhythm was restored, P-R conduction time was prolonged to 0.24 second Occasional auricular premature contractions were recorded.

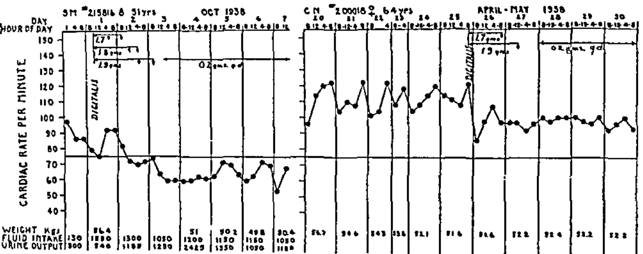


Fig. 10

Effect of Digitalis Leaf (New York Heart Association) on Two Patients with Normal Rhythm

A· Slowing of heart rate to normal levels in a man 51 years of age when 1.7 to 1.8 Gm. of the drug had been given orally. Maintenance dose was 0.2 Gm.

B· Slowing of heart rate in a woman 64 years of age with 1.7 Gm. of the drug in 24 hours. The slowing was marked and definite but the rate did not reach normal levels. Maintenance dose was 0.2 Gm. The digitalizing amount of this preparation was 1.8 Gm.

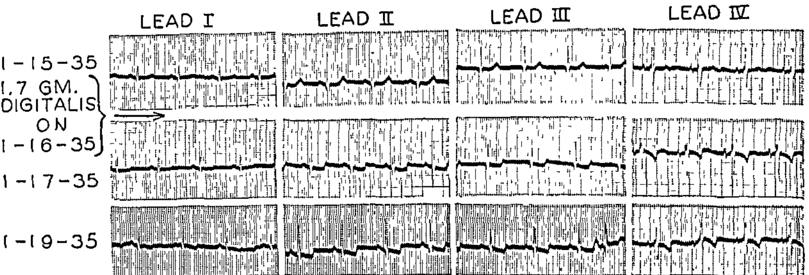


FIG 12

Effect of Digitalis in the Presence of Normal Rhythm, in a Man of 69 Years Suffering from Arteriosclerotic Heart Disease. Electrocardiogram taken January 15, 1935 served as a control record Digitalis leaf 1.7 Gm was given on January 16. Electrocardiogram taken 24 hours later showed the alterations in the form of the T waves in all leads. $T_{1,2,3,4}$ had decreased in amplitude and had become negative and showed typical digitalis configuration. Electrocardiogram taken on January 19 showed that the heart rate was slower and the T waves were somewhat more negative in Leads I, II and III and had decreased in amplitude in their positive phase. There was a single auricular premature contraction in Lead III.

or by the intravenous route, provided it is given within 24 hours. Nor does there appear to be any significant difference if the full amount is given at one dose or in broken doses. However, while 1.8 mg. has been given orally in one dose in order to ascertain its effects, this method of administration is not recommended as a routine procedure. The average daily *maintenance* amount, determined in the same manner as that used for the whole leaf, is around 0.15 mg. These matters will be further elaborated under Clinical Use and Dosage (page 71).

CLINICAL EFFECTS OF DIGITALIZATION

The following effects of digitalization have been observed in subjects with normal hearts as well as in those with abnormal hearts.

Ventricular Rate and Pulse Deficit

In the presence of auricular fibrillation slowing of the ventricular rate and decrease in pulse deficit comprise two of the most dramatic benefits of digitalization (Figs. 5, 6, 7, and 9). These effects come about because the drug increases auriculoventricular block, so that fewer excitation waves arrive at the ventricles.

Normal Sinus Rhythm and P-R Conduction Time

With normal sinus rhythm slowing of the heart from vagal stimulation may be moderate or marked (Fig. 10). In large amounts digitalis preparations increase the P-R conduction time in the electrocardiogram when normal sinus rhythm is present (Figs. 11 and 31*B*). Conduction effects are not usually seen, however, after therapeutic amounts. Prolongation of the P-R or first-degree heart block may be recorded. Partial heart block occurs with larger amounts since excitation waves from the sinus node are prevented from reaching the ventricles, this phenomenon may take place only occasionally or it may be seen in a fixed pattern (Fig. 31*C*). Finally, with more marked intoxication complete heart block—complete auriculoventricular dissociation—may occur (Figs. 11 and 31*I*).

T Waves and RS-T Segments

Alterations of the T waves and RS-T segments of the electrocardiogram are ordinarily seen after the administration of digitalis. The T waves may decrease in amplitude or become diphasic or wholly negative, or negative waves may become less negative. The RS-T segments commonly take on a characteristic configuration (Figs. 7 and 12). The changes in T waves may appear at any time in the course of digitalization.

All of the foregoing effects may be slight to insignificant, or marked, even when the same amount of digitalis preparation is given. The magnitude of the changes bears no relation to either the amount of the drug or the therapeutic effect.

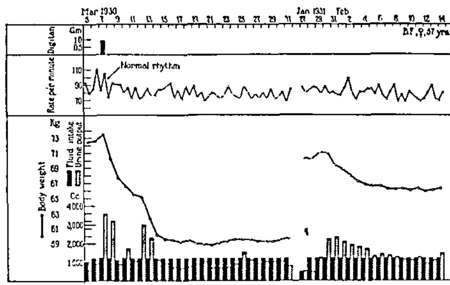


Fig 14

Dr Thomas M. Rivers, Director of the Hospital of the Rockefeller Institute for Medical Research)

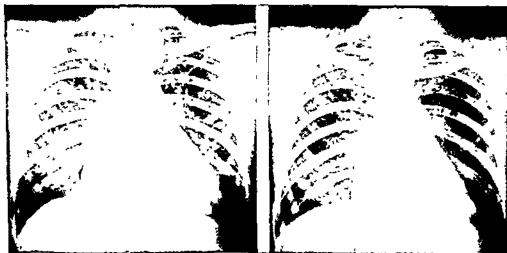


Fig. 15.

and Wheeler, C H · Action of digitalis in uncompensated heart disease. *Arch. Int. Med* 62·569, 1938)

Extent and Force of Contraction

Digitalis exerts an effect on contraction which is recorded by roentgenokymograms as an increase in extent of contraction Still another effect of digitalis has been recorded experimentally in strips of cat heart muscle, namely an increase in the force of contraction, but this action does not appear to be a crucial effect of digitalis If it were, increase in cardiac output would be expected from the normal

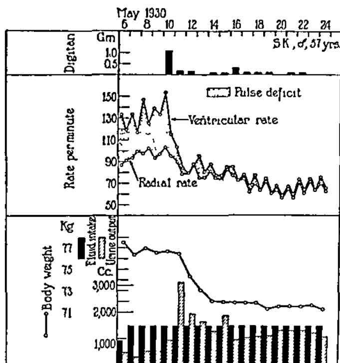


Fig. 13.

Effects of Digitalis (Digitan) Orally in 57-Year-Old Man with Congestive Heart Failure and

tute for Medical Research for permission to use these data)

heart as from the failing heart. It has been repeatedly shown, however, that digitalization decreases the cardiac output in normal subjects. When a patient is digitalized over a period of 24 hours the heart sounds may become louder, giving the observer the impression that the organ is contracting more forcibly.

Urine Output

Increase in urine output may occur when the drug is given to patients with heart failure, and loss of body weight may ensue, not only in patients with auricular fibrillation (Fig 13) but also in those with normal rhythm (Fig 14). The mobiliza-

tion of fluid resulting in this diuresis is brought about by improvement in cardiac function, with consequent improvement in renal circulation; it is not due to a direct effect of digitalis on the kidneys

Up to this point all of the observations described have been clinical ones which can be made easily. Fuller observations with respect to the effect of digitalis preparations on cardiac output and size require special technics. These have been carried out by different investigators in sufficiently large series of patients to make the patterns reasonably clear.

Cardiac Output and Size

In Normal Hearts

The administration of digitalis to subjects with normal hearts decreases the size of the heart, decreases the cardiac output, and prolongs the circulation time.

In Congestive Heart Failure

When digitalis is given to patients suffering from heart failure the cardiac size decreases (Fig 15), the cardiac output which was low beforehand increases; the circulation time is shortened, and the venous pressure falls. Stewart and his associates showed that these effects were recorded not only in patients with normal sinus rhythm (Figs. 15 and 16), to whom whole leaf was given, but also in those with auricular fibrillation (Fig 17). In their studies the Grollman technic for measuring cardiac output was employed Recent studies using the technic of right heart catheterization have given similar results for certain of the digitalis glycosides. For instance, Bloomfield and his associates have found that intracardiac administration of 0.25 to 0.75 mg. of *ouabain* to patients suffering from nonvalvular types of heart disease resulted in rise in stroke volume within one to eight minutes Patients with auricular fibrillation as well as those with normal rhythm were represented in the study

Stead and his associates have made similar observations relating to *lanatoside* C The intravenous injection of 1 6 mg of this glycoside in patients with congestive failure accompanying normal rhythm resulted first in fall in atrial pressure, then in an increase in cardiac output which averaged 1.6 liters per minute. Effects were recorded as early as 50 minutes after injection of the drug. These investigators calculated that the increase in cardiac output represented an increase in blood flow to the tissues of 2300 liters per day.

Richards and his associates have shown that *digoxin* increases the cardiac output in patients with heart failure The rise in output was accompanied by a marked fall in pulmonary artery pressure, probably reflecting decrease in auricular pressure. This effect was observed 10 to 20 minutes after the drug was given.

All these investigators have interpreted the increase in cardiac output as due to an action of the drug on the heart muscle.

Before the Onset of Heart Failure

When digitalis is given to patients with organic heart disease before the onset of failure, the results in some are like those in normal subjects, in others they are

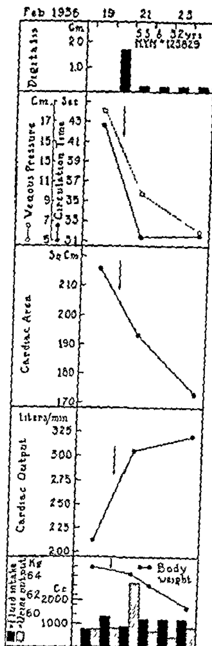


FIG 16.

Effects of Digitalis in a Man of 32 Years Suffering from Rheumatic Heart Dise
Heart Failure, with Normal Rhythm During failure cardiac output was lo
venous pressure elevated, and the heart large With administratio
1 8 Gm in 24 hours cardiac outp

tion of fluid resulting in this diuresis is brought about by improvement in cardiac function, with consequent improvement in renal circulation; it is not due to a direct effect of digitalis on the kidneys.

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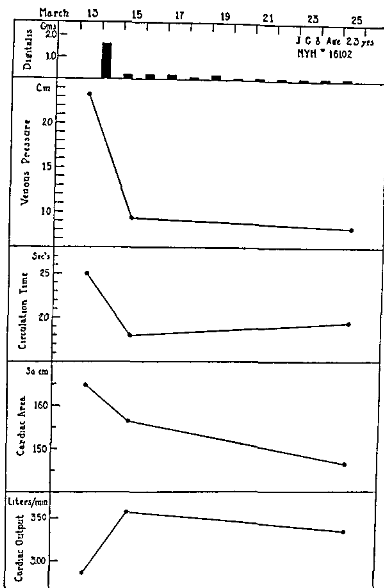


Fig 17

Effect of Digitalis in a 23-Year-Old Man Suffering from Rheumatic Heart Disease, with Congestive Heart Failure and Auricular Fibrillation Before digitalization cardiac output was reduced, venous pressure elevated, circulation time prolonged, and the heart large After 1 8 Gm digitalis leaf (New York Heart Association preparation) in 24 hours there was increase in cardiac output,

like those of patients with heart failure, in still others there is no change either in heart size or output, or in circulation time.

Interpretation of Action of Digitalis

One interpretation of the effect of digitalis is shown in Fig. 18. It appears that the effect of the drug on the size of the heart is critical, since there is no change in cardiac output unless change in size occurs. The normal heart—and, prior to the occurrence of failure, certain damaged hearts—are made smaller

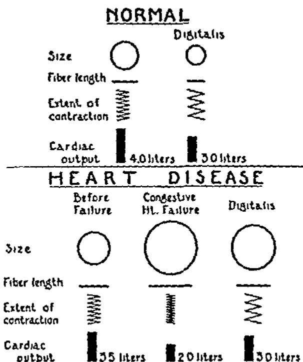


Fig. 18.

Effects of Digitalis in Normal Subjects and in Patients with Heart Disease before Failure, during Failure, and after Administration of Digitalis

pumps, consequently their output is reduced. In the failing, dilated heart the shortening of the stretched fibers makes them approach more nearly an optimal length so that the heart size decreases and the output increases; certain compensated hearts behave like the normal hearts while others follow the pattern of failing hearts, it being clinically impossible to separate these groups. It seems that the human heart obeys Starling's Law, which states that the *cardiac output increases with the dilatation of the heart and with the increase in length of muscle fibers. As stretching proceeds and becomes greater, the length of the fibers exceeds* their optimal length and the output decreases.

CLINICAL USE AND DOSAGE

In most patients when it has been decided to use the whole digitalis leaf or digitoxin I recommend that digitalization be carried out within 24 hours if the patient is in bed. In this case excretion of the drug during this period can be neglected. If, on the other hand, it is undertaken more slowly, allowance must be made for excretion as well as for digitalization. If the patient remains ambulant, digitalization should not be attempted within 24 hours, but spread over several days (p. 95).

Whole Leaf

The whole leaf preparation of digitalis—derived from *Digitalis purpurea*—is adequate and satisfactory for the digitalization and maintenance of most patients. The purified glycosides do not result in safer or more effective digitalization, and maintenance over long periods may not be so well obtained. Batterman and DeGraff have shown that if a patient is not being maintained satisfactorily on digitalis leaf and toxicity occurs with the next increment of dosage, the *substitution of a digitalis glycoside will result in toxicity if comparable doses of the* latter are used.

In the face of these facts there appears to be no reason to give up the whole powdered leaf as a therapeutic agent. It can be used on most occasions if the patient is not nauseated and is not vomiting, and if there is no need for a more rapidly acting preparation.

Dosage in Auricular Fibrillation

If the patient with auricular fibrillation has not had digitalis beforehand a tentative schedule can be set up to give 1.8 Gm. (U.S.P. XIV) within 24 hours in the following doses. 0.8 Gm. at once, 0.5 Gm. in four to five hours, 0.3 Gm. four to five hours later, and 0.2 Gm. four to five hours later still. Any one dose may be omitted if nausea and vomiting have appeared or if the ventricular rate has fallen to 60 to 65 beats per minute (Figs. 5 and 6). Cognizance is also taken of ventricular premature contractions, and of nausea and vomiting, as manifestations of heart failure which may disappear upon adequate digitalization. The ventricular rate is the key to dosage—if appropriate slowing has not taken place, additional amounts of the drug should be given.

If the patient has had digitalis but the amount is not known, appropriately smaller amounts than those just mentioned should be given. A total dosage of 1.5 Gm. or less in the first 24 hours may be sufficient. Here, too, the rapidity of the fall in ventricular rate remains the guide.

If the physician has had experience with the preparation and knows what it will do, the full digitalizing amount can be given in one dose if it appears necessary, but this course is not recommended for routine use because of the possibility of nausea and vomiting.

After the rate has been slowed maintenance doses are instituted, usually around 0.2 Gm. daily, the aim being to hold the resting ventricular rate at approximately

70 beats per minute. The ration dose varies from patient to patient. The average maintenance dose of the whole leaf preparation (U.S.P. XIV) is 0.2 Gm. per day, but 0.1 Gm. alternating with 0.2 Gm. per day may be required, or 0.2 Gm. alternating with 0.3 Gm. In a few patients 0.1 Gm. or less may be sufficient, or 0.3 Gm. or more may be required daily.

Dosage in Normal Sinus Rhythm

The same amounts of digitalis are given to patients with normal sinus rhythm as to those with auricular fibrillation (Figs. 10 and 16). The ventricular rate does not serve as a guide in these patients with normal sinus rhythm, although the same precautions are observed as in the patients with auricular fibrillation. In the first 24 hours average amounts are given, namely 1.8 Gm. over this period. The average ration amount is 0.2 Gm. Electrocardiograms should be taken occasionally when digitalis whole leaf is given over a long time, to detect prolongation of the P-R conduction time, which is seen occasionally.

Dosage in Auricular Flutter

When the whole leaf is given in the treatment of auricular flutter amounts greater than the usual therapeutic ones may be required to bring about reversion to normal rhythm. This drug is given in the manner already described, except that larger amounts are given toward the end of the first 24 hours if reversion has not occurred, and more than maintenance amounts the next day and the day following, until reversion or nausea and vomiting occur. Amounts larger than the *therapeutic ones may also be required in the presence of auricular and auriculo-*ventricular tachycardia (see Lanatoside C, p. 77).

Dosage and Effects in Congestive Heart Failure

The heart rate usually declines when the whole leaf is given in the treatment of heart failure but the slowing is more dramatic when auricular fibrillation is present than when normal rhythm prevails. Within a few hours dyspnea is less marked, the patient becomes more comfortable, cyanosis may decrease, the patient may become drowsy and fall asleep, nausea may diminish, and diuresis begin. Upon auscultation the heart sounds are more forceful. Improvement proceeds as fluid is mobilized. Indeed the patient may become free of the signs and symptoms of heart failure by means of this drug alone.

Unless there is urgency I digitalize patients with congestive heart failure in 24 hours according to the plan given above and observe how much benefit is derived from this measure before using mercurial diuretics.

Digitoxin

Digitoxin is a glycoside derived from *Digitalis purpurea* leaf. It can also be obtained from hydrolysis of lanatoside A. It can be prepared in pure form. Nevertheless, according to a survey by Dick, the potency of various digitoxin preparations has been found to vary considerably. Because of this variation Dick urged that the whole leaf should be retained for routine digitalization. After extensive use in

many clinics, the range of usefulness of this drug is now understood and its use more clearly defined.

Oral Dosage

It appears that 1.8 to 2.0 mg. if given orally within 24 hours is the average amount required for adequate slowing of the ventricular rate in patients with auricular fibrillation (Figs. 8 and 9). The total amount may be distributed as follows: 0.8 mg. as the initial dose, followed in four to five hours by 0.5 mg., by 0.3 mg four to five hours later, and by 0.2 mg. four to five hours later still. In those patients for whom more is required the additional amounts have no relation to body weight. A total dose of 1.2 mg. which has been advocated by Gold is insufficient to achieve adequate slowing in most patients (Fig. 8). Gold himself states that he has not made observations of the number of patients adequately digitalized by this amount. The average amount which I recommend can be applied to the treatment of patients with normal sinus rhythm in the manner similar to that described for establishing the digitalizing amount of the whole leaf. The absorption of digitoxin by the oral route proceeds at about the same rate as that of the whole leaf, if the slowing of the ventricular rate is used as a guide. *The average maintenance dose of digitoxin daily* is between 0.1 mg and 0.2 mg. A ration amount of 0.2 mg is excessive for most patients after adequate digitalization. Many patients may be adequately maintained on 0.1 mg. daily; a few may require as much as 0.3 mg.

Dosage by the Intravenous Route

Digitoxin can be given intravenously. It affects the ventricular rate, however, only slightly more rapidly than when administered orally. The drug has the same effect within 24 hours if given in one dose or in divided doses, intravenously or by mouth. However, the drug should only be given intravenously when necessary. It should be diluted with normal saline because it is dissolved in approximately 40 per cent alcohol. One cubic centimeter of the solution is equivalent to 0.2 mg of digitoxin. The total amount for digitalization, 1.8 mg., is divided as for oral administration, since it is not safe to give the total digitalizing amount in one dose. The intravenous maintenance amounts are the same as the oral rations.

Advantages and Disadvantages

In the first place, digitoxin has the advantage of being obtainable in pure form. Secondly, it is suitable for intravenous use, and the route of administration can be changed during the process of digitalization. The drug seems to be absorbed as completely from the gastrointestinal tract as when it is given by vein. The intravenous preparation finds application in patients who are nauseated and are vomiting, and in surgical or other patients in whom the oral administration of digitalis is not possible, or when no other intravenous preparation is available to secure a more rapid effect.

But digitoxin is not without its disadvantages:

When this preparation is given orally it has no appreciable advantage over the whole leaf in speed of digitalization.

When adequate amounts are given to achieve slowing of the ventricular rate in the presence of auricular fibrillation, nausea and vomiting occur more frequently than in the case with the whole leaf.

It is more difficult to maintain patients on digitoxin than on the whole leaf. When toxicity occurs it may be of long duration. Symptoms may persist for a week or ten days because of the slow rate of dissipation of the drug. Master has called attention to the frequency of intoxication from digitoxin in its routine use. Stone has reported auricular tachycardia with auriculoventricular dissociation following 1.2 mg. digitoxin in one dose. I have seen auricular paroxysmal tachycardia with 2:1 block or complete auriculoventricular dissociation occur so frequently following its use (Fig. 24) that I am restricting the occasions on which it is given.

If toxicity occurs during maintenance with the whole leaf, digoxin, or lanatoside C, these drugs need not be discontinued in all instances; toxicity may disappear if a smaller dose is given. On the other hand, when toxicity occurs with digitoxin, the drug should be discontinued until the symptoms and signs of overdigitalization disappear, since digitoxin is excreted slowly, and continued administration may prolong the toxic effect.

Other Glycosides

The other digitalis glycosides have not had the intensive study that has been accorded digitoxin. The amounts required for adequate digitalization and maintenance have not been established as accurately as has been the case for the whole leaf and for digitoxin. Differences in objectives in various studies and in the manner of giving the drugs make it difficult to decide upon dosage.

The preparations of digitalis available for oral and intravenous use, as well as the range of dosages and the times certain effects appear, have been brought together in Tables I and II.

Digoxin

Digoxin is a pure glycoside obtained from *Digitalis lanata* leaf. It can also be obtained from lanatoside C. Digoxin has a place of usefulness for a few patients. The average oral digitalizing amount is approximately 3.75 mg., given in divided doses. The average maintenance dose is 0.75 mg. The effects of oral digoxin can be detected in one to two hours, that is, not quite so rapidly as is the case with lanatoside C, and is maximal in three to four hours. Richards and his associates have shown that it increases the cardiac output 10 to 20 minutes after intravenous injection. Since it is excreted in 24 to 36 hours, toxicity is of short duration. DeGraff thinks its relatively short latent period and its rapid dissipation rate make this drug a useful one for the rapid oral digitalization and daily maintenance of patients with congestive heart failure. Intravenous use of this drug is not practical, since it is relatively insoluble, large quantities of fluid have to be injected in order to give the required amount of digoxin. Intravenous dosage would be 1.0 to 1.5 mg.

Table I. Digitalis Preparations for Oral Use

Preparation	Digitalizing amount in 24 hours	How to spread doses	Maintenance amounts daily		How soon effect detected on cardiac output, on slowing of the ventricular rate in auricular fibrillation, and in fall of venous pressure (latent period)	How soon maximum effect secured	How soon excreted—rate of dissipation
			Average	Average range			
Whole leaf (U.S.P. XIV)	1.8 Gm	0.8 Gm, 0.5 Gm, 0.3 Gm, 0.2 Gm, at 4- to 5-hour intervals	0.2 Gm	0.1 Gm to 0.3 Gm.	1 to 2 hours	24 hours	2 to 3 weeks
Digitoxin	1.8 to 2.0 mg	0.8 mg, 0.5 mg, 0.3 mg, 0.2 mg, at 4- to 5-hour intervals	0.15 mg (0.1 mg alternating with 0.2 mg. daily)	0.1 mg every 2 days to 0.1 to 0.3 mg or more	1 to 2 hours (Same as digitalis leaf)	24 hours	2 to 3 weeks
Digoxin	3.0 to 3.75 mg, 2.0 to 5.0 mg *	Divided doses	0.75 mg by mouth	0.50 to 0.75 mg up to 1.0 mg every day	1 to 2 hours	4 hours if given in 1 dose (24 hours if spread over 24 hours)	24 to 36 to 72 hours

Lanatoside C	7 0 mg in 24 hours 16 0 mg in 72 hours	Divided doses	1 0 mg	0 5 to 1 0 mg		24 hours if spread over 24 hours	72 hours
Gitalin (amorphous)	5 7 mg (range 3 0 to 10 5 mg)*	2 5 mg initial dose followed by 0 75 mg every 6 hours until therapeutic effect	0 5 mg	0 25 to 1 25 mg	Shorter than digitoxin		
Urginin (Squill, Scillaren) (digitalis-like action)	1 5 mg t i d for 2 days followed by 1 0 mg. b d until desired effect is obtained. Average total effective amount over several days is 9 0 mg, range from 6 5 to 14 mg.†		1 0 mg	0 5 to 2 0 mg			8 to 11 days

* DeGraff
† Chamberlain and Levy.

Table I. Digitalis Preparations for Oral Use (Continued)

Preparation	Duration of toxic effects	Prominent toxic effects	Evaluation	Range in strength from preparation to preparation
Whole leaf (U S P XIV)	24 to 48 hours		Best preparation for routine digitalization and maintenance of patients requiring digitalis	Varies but clinical strength should be tested on patients with auricular fibrillation
Digitoxin	1 to 10 days	Abnormal rhythms, auricular paroxysmal tachycardia, 2 1 auricular paroxysmal tachycardia	Not a satisfactory preparation for routine digitalization and maintenance Toxic effect more common when digitalization is adequate than with whole leaf Maintenance is more difficult than with whole leaf	Said to vary in the different preparations available, but should be constant if pure.
Digoxin	Very short since rapidly dissipated		Satisfactory for rapid oral digitalization and maintenance because toxicity is of short duration due to rapid dissipation.	
Lanatoside C	36 hours		Maintenance is difficult Not very satisfactory for oral digitalization	
Gitalin (amorphous)	Shorter than digitoxin		Therapeutic dose about one third of toxic dose.	Said to be uniform.
Urginin (Squill, Scillaren) (digitalis like action)		Nausea and vomiting, diarrhea, transient auricular fibrillation, auriculoventricular block, no ventricular premature contractions	Useful for patients in whom digitalis induces nausea and vomiting and for patients prejudiced against digitalis	

Gitalin (Amorphous)

Gitalin (amorphous) is a mixture of glycosides obtained from the aqueous extract of *Digitalis purpurea*. The drug appears to run uniform from batch to batch It has a latent period shorter than digitoxin but longer than digoxin. Its rate of dissipation is not as slow as digitoxin or digitalis leaf and not as rapid as digoxin or lanatoside C (*Batterman and DeGraff*). *Gitalin is given orally. The average digitalizing dose is* 5.7 mg. when digitalization is carried out by the multiple-dose method in 24 to 48 hours, the range being 3 0 to 10 5 mg (Batterman and DeGraff). An initial dose of 2 5 mg. may be followed by 0.75 mg. every six hours until the desired effect is obtained. About three-quarters of patients require 0.5 mg. or less for daily maintenance after digitalization, the range being 0 25 to 1 25 mg. Amorphous gitalin 0.5 mg. appears to be equivalent to 0 1 Gm. digitalis leaf in terms of therapeutic effect

When patients cannot be given adequate amounts of other preparations of digitalis to achieve therapeutic digitalization without toxicity gitalin might be used, since its therapeutic dose appears to be only one-third of the toxic dose, contrasted with two-thirds of the toxic dose for digitalis leaf, digitoxin, digoxin, and lanatoside C.

Lanatoside C

Lanatoside C is a crystalline glycoside obtained from *Digitalis lanata* leaf It has a wide field of usefulness for rapid intravenous digitalization It has a short latent period, almost as short as that of ouabain, its effects on increase in cardiac output are apparent in one-half to one hour after injection, and are maximal one to two hours after injection Venous pressure falls within five minutes (an effect which is maximal at 30 to 60 minutes) Lanatoside C is rapidly excreted (within about 72 hours)—not so rapidly as is ouabain.

The average amount for intravenous digitalization is 1 6 mg Given orally, about 7 0 mg. are required The oral maintenance doses vary from 0 5 to 1 0 mg The range between therapeutic and toxic doses may be small in some patients It is not recommended for routine oral use nor for maintenance. In a few patients for a few days we have used between 0 2 and 0 4 mg intravenously as the maintenance dose Lanatoside C is especially useful in the treatment of acute heart failure, auricular flutter, and supraventricular paroxysmal tachycardias.

Ouabain

Ouabain (G strophanthin) is a pure crystalline glycoside derived from *Strophanthus gratus* It is used intravenously because it is not absorbed adequately from the gastrointestinal tract On account of the brief latent period of this drug, slowing of the ventricular rate in auricular fibrillation can be detected within a short time after its injection

If the patient has had no digitalis for two weeks beforehand, 0 5 mg. can be given intravenously and followed at one-half hour to one-hour intervals by 0 1- to 0 2-mg amounts until a total of 1 0 mg has been given The maximal effect from the total digitalizing amount is apparent in one to two hours This drug is excreted

Table II. Intravenous Digitalis Preparations

Preparation	Digitalizing amount in 24 hours	How to spread doses	Maintenance amounts daily: Average	Maintenance amounts daily: Average range	How soon effect detected on cardiac output, on slowing of the ventricular rate in auricular fibrillation, and in fall of venous pressure (latent period)
Ouabain	1.0 mg, 0.7 to 1.0 mg. (DeGraff)	0.5 mg followed by 0.1 mg every ½ hour	0.7 to 1.0 mg, has to be repeated every day intravenously		Lowering of venous pressure in 1 to 8 minutes (1)†
Lanatoside C	1.6 mg	1.6 mg. in one dose* or 0.8 mg. followed in 2 hours by 0.4 mg and 2 hours later by 0.4 mg	1.0 mg orally or 0.2 to 0.4 mg intravenously	0.5 to 1.0 mg. orally or 0.2 to 0.4 mg intravenously	Effect on cardiac output in ½ to 1 hour (2)† (short as ouabain); effect of venous pressure (lowering) in 5 to 10 minutes and continued for 30 to 60 minutes
Digoxin	1.0 to 1.5 mg		0.75 mg. orally		1 to 2 hours. (Slightly longer than lanatoside C) (3)†
Digitoxin**	1.8 to 2.0 mg.¶	0.8 mg, 0.5 mg, 0.3 mg, 0.2 mg at 4 to 5 hour intervals 1.2 mg may often be given at first dose without toxic effect	0.15 mg. intravenously or orally	0.1 to 0.3 mg. or more intravenously or orally	1 to 2 hours (4)† (May be slightly faster than by mouth)
Acetyl strophanthidin (digitalis like action)	1.0 to 1.2 mg	0.5 mg. followed by 0.25 mg. 10 minutes later and so on at 10 minute intervals until therapeutic objective or until minor toxic symptoms	Not suitable; effect too transient		1 to 5 minutes (1)†

† (1), (2), (3), (4), is the order of latent period, (1) being the shortest
* 0.4 mg may stop paroxysmal auricular fibrillation.
** For intravenous use digitoxin should be diluted with normal saline because it is dissolved in 40 per cent alcohol 1.0 cc of the solution is equivalent to 0.2 mg
¶ Reason for using because constant but different preparations of different manufacturers differ Dick, Brit Heart J 10 122, 1948
‡ I, II, III refer to order of dissipation rate, I being the shortest

Preparation	*How soon maximum effect secured*	*How soon excreted (rate of dissipation)*	*Duration of toxic effects*	*Prominent toxic effects*	*Evaluation*
Ouabain	1 to 2 hours	24 hours (I)‡	Short		Useful for rapid digitalization and then shift to another preparation Not suitable for maintenance as it is rapidly excreted Poorly absorbed by mouth and has to be given intravenously
Lanatoside C	½ to 2 hours to 3 hours	72 hours (II)‡, not so fast as ouabain	36 hours		Range between toxic and therapeutic doses is small Not satisfactory for maintenance.
Digoxin	2 hours (3)	72 hours (II)‡	Short		Poorly soluble, therefore not easy to give intravenously. If put up in 70 per cent alcohol ampules it has to be diluted with sterile distilled water
Digitoxin**	24 hours	2 to 3 weeks (III)‡	1 to 10 days	Same as by mouth	Useful when patient is nauseated and is vomiting or cannot take oral digitalis and when rapid digitalization is not required. Should shift to oral leaf as soon as possible, since maintenance is difficult and toxicity occurs.
Acetyl-strophanthidin (digitalis-like action)	15 to 20 minutes	1 to 3 hours (I)‡	Short	Ventricular paroxysmal tachycardia and ventricular fibrillation	May be useful for rapid digitalization in pulmonary edema or for paroxysmal tachycardia but too toxic for clinical use.

within 24 hours. It is useful for rapid digitalization especially in acute heart failure but is not suitable for maintenance.

Drugs With Digitalis-Like Action

Acetyl-Strophanthidin

Acetyl-strophanthidin is a rapidly acting digitalis-like substance which has been studied by Gold *et al* and Enselberg *et al.* Its effects when given intravenously are apparent in five minutes, and are at a maximum in 15 to 20 minutes. It is excreted within one to three hours; accordingly toxic effects are of short duration. A total dosage of about 1.0 to 1.2 mg. may be expected to complete digitalization on patients with auricular fibrillation, as shown by the ventricular rate. Gold *et al.* gave 0.5 mg. as the initial dose, following it at ten-minute intervals with 0.25 mg amounts until the therapeutic objective was gained or minor toxic symptoms appeared

Enselberg *et al.* found that: (1) acetyl-strophanthidin slowed the ventricular rate in patients with auricular fibrillation, but not consistently; (2) it restored supraventricular paroxysmal tachycardias to normal rhythm rapidly; but (3) acute intoxication, the most serious being ventricular paroxysmal tachycardia and ventricular fibrillation, occurred in one out of every four patients. The toxic effects were of short duration. They concluded that this drug should not be used in clinical practice at this time

Squill, Scillaren—Urginin

I have had no occasion to use squill The active principle of this drug with digitalis-like effects can be obtained under the trade name of Urginin * It is a mixture in approximately equal proportions of two of the active water-soluble glycosides—crystalline scillaren A and amorphous scillaren B.

A study of Urginin has been made by Chamberlain and Levy. They found that it exerted an action similar to that of digitalis in patients with heart failure in the presence of normal rhythm and of auricular fibrillation The dosage they recommended was 1.5 mg orally, three times a day for two days, followed by 1.0 mg twice a day until the desired effect was produced, if no digitalis or Urginin had been given for ten days Toxic effects were nausea, vomiting, diarrhea, transient auricular fibrillation, auriculoventricular nodal rhythm, and varying degrees of heart block Premature contractions were not encountered The effects demonstrated in electrocardiograms were similar to those attributed to digitalis The investigators concluded that *Urginin was effective* but that it had no advantages over digitalis They thought it might be useful for patients in whom digitalis induced nausea and vomiting, and for patients who had a prejudice against digitalis.

INDICATIONS AND CONTRAINDICATIONS

The indications for digitalization are clear-cut in most instances. The use of the preparations described in the treatment of congestive heart failure, abnormal

* Calco Chemical Co, Inc.

rhythms, and in other appropriate situations is given in the relevant chapters. For the sake of convenient reference, however, indications and contraindications are summarized briefly here.

Indications

Heart Failure

Congestive heart failure is the most common indication for digitalization. The use of digitalis is indicated:

1. whether the rhythm is normal sinus mechanism or that of auricular fibrillation or other abnormal rhythms—ventricular paroxysmal tachycardias being the exception;
2. whatever the etiology of the heart disease,
3. whatever the anatomic defect of the cardiac muscle or valves, and whether the damage is acute or chronic if the heart is failing,
4. in acute episodes of heart failure such as pulmonary edema and nocturnal dyspnea;
5. in acute heart failure during or after surgical operations;
6. when acute heart failure occurs in obstetric cardiac patients as a result of respiratory infection or increased strain on the heart by anesthesia, increase in blood volume, or the work of labor,
7. when heart failure occurs in pulmonary embolism or in collapse of a lung;
8. in acute myocarditis with congestive heart failure, whether it is due to rheumatic fever, Fiedler's myocarditis, virus infection, or other agents;
9. in congestive heart failure which may have been precipitated by the onset of auricular fibrillation or other abnormal rhythms,
10. in myocardial infarction, not only if signs of heart failure appear but also if auricular fibrillation or one of the paroxysmal rhythms occur for which it may be appropriate,
11. when ventricular paroxysmal tachycardia is present, but only if quinidine or procaine amide hydrochloride has not terminated the rhythm, and the treatment of heart failure becomes of greater concern than the possibility of the toxic effect of digitalis in the presence of the tachycardia,
12. in myocardial failure with pulsus alternans, in which digitalization may eliminate the inequality of the radial pulse beats,
13. in early heart failure with moderate dyspnea or a few basal râles

In the treatment of certain patients it may not be possible to orient all the factors which play a part in the symptoms Consequently it may be in order in such instances to test the effect of digitalis in the relief of the symptoms For instance, fatigue and weakness may occasionally be due to early myocardial insufficiency without any evidence of congestive phenomena

Auricular Fibrillation

Digitalis is used in the treatment of auricular fibrillation to slow the ventricular rate whatever the etiology of the auricular fibrillation or the circumstances under which it occurs (Figs. 5 and 7) If there is failure digitalization serves a double purpose.

SLOW VENTRICULAR RATE. In a few patients with auricular fibrillation the ventricular rate is slow and it remains slow with exercise even without digitalis Moreover, the patient remains free of heart failure Digitalis need not be given to such patients provided close supervision is maintained in order to detect rise in ventricular rate and the onset of heart failure.

CHRONIC CONSTRICTIVE PERICARDITIS. In chronic constrictive pericarditis when auricular fibrillation occurs digitalis is used to keep the ventricular rate slow, but it is not indicated in the presence of normal sinus rhythm

HYPERTHYROIDISM. When auricular fibrillation occurs in hyperthyroidism, with or without heart failure, digitalis is given to slow the ventricular rate to the optimal range.

Auricular Flutter

A digitalis preparation is the drug of choice in the treatment of auricular flutter with or without failure or whatever the etiology. In a few instances the ventricular rate *is slow because of high-grade auriculoventricular block. There may be no* evidence of heart failure. Digitalization is not indicated at such a time unless the decision is made to attempt conversion to normal sinus mechanism Lanatoside C may be the drug of first choice when a rapid effect is essential.

Auricular and Auriculoventricular Paroxysmal Tachycardias

Digitalis is the drug of choice in the treatment of most instances of auricular and auriculoventricular paroxysmal tachycardias (for pronestyl see pp. 161 and 178–179). Lanatoside C may be especially useful in the treatment of these rhythms when a rapid effect is desirable.

Auricular Premature Contractions

Digitalis may be effective in eliminating auricular premature contractions which give rise to symptoms.

Heart Block

COMPLETE HEART BLOCK. When heart failure is present in a patient with complete heart block, and the block is not due to an effect of digitalis, this drug is indicated. However, the block must have been stabilized and Adams-Stokes attacks must not be occurring. Occasionally, however, digitalization may prevent Adams-Stokes attacks (p. 168).

PARTIAL HEART BLOCK. When heart failure prevails digitalis is indicated in the presence of partial heart block, namely in first- and second-degree heart block, provided the block has not been due to this drug. In organic heart block the degree of block is not increased by digitalization since the effects are not additive.

Patients with Large Hearts and *Organic Heart Disease Before the Onset of Heart Failure*

Christian has suggested the use of digitalis in patients with heart disease prior to the onset of heart failure, in order to prevent the occurrence of failure and delay further enlargement of the organ. *Stewart and his associates have shown that*

digitalis decreased the size of the heart and increased the output in certain patients with organic heart disease before the onset of failure—a response similar to that observed in heart failure. In other patients with the same functional clinical classification digitalization decreased the heart's size but it also lowered the volume output of blood from the heart per minute: In short, a response occurred which duplicated that observed in normal hearts. The work accomplished by the heart per beat in relation to its size was increased in spite of the decrease in output, so that the work was more nearly commensurate with the size of the organ These data give an objective basis for Christian's clinical impression.

Later Erickson and Fahr showed that compensated patients with organic heart disease showed improvement in mechanical efficiency (work) when they were digitalized, but, in contrast, subjects with normal hearts showed impairment in mechanical efficiency upon digitalization. The maximal improvement in mechanical efficiency occurred in their patients with organic heart disease in whom the circulation time, according to the technic they used, was increased to 16 to 20 seconds. As a result of these observations they thought that digitalization was indicated in compensated patients with organic heart disease when the circulation time was 16 seconds or longer. I am not aware, however, that the digitalization of compensated patients is being carried out to any great extent. Observations of a large number of patients over a long period of time would be necessary in order to determine whether the life span and life histories with respect to heart failure and other complications differ from those of patients in whom digitalis was used only in the current manner: after the onset of failure or because of irregularities of the rhythm.

Contraindications

There are few contraindications to digitalization when the clear-cut indications already cited are present. The exceptions follow.

Allergy

Proved allergy to digitalis is indeed rare I have not seen a single instance of it, although a few cases have been reported of typical allergic responses in the form of fever, pruritus, urticaria, arthritis, and edema of the face. If sensitivity can be established the drug should not be used, but even in such patients it may be possible to continue to give digitalis and counteract the allergic effects with pyribenzamine

Ventricular Paroxysmal Tachycardia

Digitalis is contraindicated in the presence of ventricular paroxysmal tachycardia. There is one exception If quinidine or procaine amide hydrochloride has not terminated this rhythm and in addition (1) heart failure is present or has appeared and the patient is getting worse and (2) other measures of treating heart failure (oxygen, aminophyllin intravenously, mercurial diuretics) have not been effective, there is no alternative to the use of this drug.

Ventricular Premature Contractions

Frequent ventricular premature contractions contraindicate the use of digitalis unless they are due to congestive heart failure, in which case they may disappear with digitalization.

Chronic Constrictive Pericarditis

Digitalization is contraindicated in chronic constrictive pericarditis in the presence of normal sinus rhythm because it may further decrease the size of the already constricted heart It is used, however, in the presence of auricular fibrillation in order to slow the ventricular rate and when supraventricular paroxysmal tachycardias arise.

Hypersensitive Carotid Sinus

Digitalis is contraindicated in the presence of the hypersensitive carotid sinus unless heart failure is present The vagal effects of the drug may either induce attacks or make them more easily induced, or it may prolong the period of standstill when the attacks occur spontaneously. In case of heart failure atropine may be used to prevent the syncopal attacks so that digitalis may be given.

Complete Heart Block with Adams-Stokes Attacks

When transient complete heart block is associated with Adams-Stokes attacks, digitalis is usually contraindicated because it may induce attacks and further slow the ventricular rate. If, however, the failure has not been alleviated by other measures, digitalization may be necessary. Occasionally digitalization prevents Adams-Stokes attacks (p. 168).

Aortic Stenosis

I do not think that digitalis is contraindicated in the presence of aortic stenosis when the drug is indicated by heart failure or other conditions.

EXCRETION OF DIGITALIS

Exact information is not available about the distribution of digitalis in the body, owing to the difficulty of accurately detecting small amounts of this drug. Digitalis, or a substance which upon concentration had digitalis-like effects in animal assay, has been found in ascitic and edema fluids in digitalized patients. Only a small amount of digitalis is secreted in the urine and the bile, and the fate of the digitalis which is destroyed is not known The rate of excretion differs for the whole leaf and for the glycosides—a matter which has been discussed earlier, and which has to be taken into account in the management of maintenance doses and avoidance of toxicity.

Geiling and associates have studied excretion and distribution of radioactive digitoxin (C^{14}) in laboratory animals In normal animals digitoxin is excreted rapidly both in the urine and the feces, for the most part not as digitoxin but some metabolic product. In the cat—relatively sensitive to digitoxin—the concentration

of digitoxin in the heart was three times that in skeletal muscle, while in the guinea pig—relatively insensitive to digitoxin—the amounts in these muscles were approximately the same. The rapidity at which intermediary metabolism of digitoxin occurred is not in accord with currently accepted teaching. The use of radioactive preparations of digitalis in suitable patients should throw light on the metabolic pathway of this important drug.

TOXICITY

General Remarks

Formerly digitalis was given until nausea and vomiting occurred. When these effects ensued it was known that digitalization had been attained. Now, however, it has been established that in most cases the maximal therapeutic effects can be achieved without nausea and vomiting

Digitalis intoxication can be prevented by establishing whether the patient has already had digitalis Every effort should be made to find out whether it has been used in the past two to three weeks, and the quantities in which it was given. When digitalis leaf was used almost exclusively it was relatively easy to learn if a patient had been taking green pills, but the tracing of digitalis medication has become more difficult with the introduction of the purified glycosides, which are dispensed as white or pink tablets I do not subscribe to the use of different-colored tablets to denote different strengths of these glycosides, many instances of toxicity have resulted because physicians as well as patients become confused by the colors and because patients have been told to take the drug by color rather than by specific amounts of the drug.

I have encountered no cases of sensitivity to digitalis preparations (see p. 83) I have many times seen patients who were said to be unable to take digitalis, and have invariably given them whatever preparations I was using at the time without evidence of special sensitivity Many patients had been inadequately digitalized and the full digitalization banished the alleged "sensitivity." In this regard it is well to bear in mind that nausea and vomiting may be manifestations of heart failure and may disappear when digitalization has been completed. Thrombopenic purpura following the use of digitoxin has recently been reported.

The notion that certain preparations of digitalis are effective while others are ineffective is probably only an inaccurate reflection of the varying rates of absorption and of dissipation

Some patients have subjective symptoms from overdigitalization. Others have none, and in them the toxic effects on the heart will be the first indication of digitalis intoxication. In still other subjects both types of toxicity will appear simultaneously Many patients take large amounts of digitalis without either variety of toxicity. It will be recalled that the maintenance amounts for some patients can be increased gradually (up to as much as 0 5 Gm daily for the whole leaf) without any evidence of toxicity Under these circumstances the patient must eliminate as much of the drug as is given for the daily maintenance.

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heart block from digitalis intoxication; the bilateral central scotomatous defects in the fields of vision disappeared five weeks after the drug was stopped and fluid intake was increased.

Cardiac Manifestations

EXCESSIVE SLOWING IN AURICULAR FIBRILLATION. Excessive slowing of the ventricular rate in patients with auricular fibrillation is one of the common cardiac signs of overdigitalization The digitalis effect prevents many of the excitation waves from reaching the ventricles.

The optimal ventricular rate for most patients is around 70 beats per minute. I set 60 per minute as the rate at which subsequent doses will not be given. Should the rate fall to, say, 50 per minute, the drug is discontinued for a day or two until the rate has increased. After digitalis has been stopped the rate may remain slow for many days, or it may rise slightly and then suddenly increase. For this reason I usually restore the maintenance amounts after a few days of withdrawal—that is, before too much of the drug has been excreted.

The slowing may go on to complete heart block (Figs. 11 and 31*I*) In such a case the auricles continue to fibrillate but the ventricles beat under the direction of the idioventricular center, which discharges stimuli in a regular, slow sequence —usually between 30 and 40 per minute. Digitalis should of course be omitted until conduction of the impulses at an appropriate rate has been restored. When digitalis is being given to a patient with auricular fibrillation, the onset of this slow (30 to 40) rate with regular ventricular sequence should permit the diagnosis of complete heart block even without an electrocardiogram.

The undue weakness which LaDue described in digitalis intoxication can be accounted for by a slow heart rate during heart block which resulted in decreasing the cardiac output.

VENTRICULAR PREMATURE CONTRACTIONS. These, too, are among the common cardiac signs of digitalis intoxication. But it is recalled that ventricular premature contractions may be due to heart failure and may disappear with adequate digitalization. When they are due to administration of the whole leaf the drug should be decreased in amount or even omitted for a few days; digitoxin should be omitted completely, to allow for excretion of some of the drug. In the presence of low serum potassium the heart muscle may be more sensitive to the available digitalis so that ventricular premature contractions or forms of heart block may result, in the absence of overdigitalization. The administration of potassium will correct this.

The premature contractions may occur occasionally, frequently, or in a regular pattern. The most common pattern is that in which they occur after every second beat, giving rise to coupling, or bigeminy (Fig. 32). Although this is seen in patients with normal rhythm it is more frequent in those with auricular fibrillation. Digitalis should be discontinued until coupling has disappeared. In auricular fibrillation it is often impossible to maintain an appropriate level of ventricular rate without occasional ventricular premature contractions, especially if the heart is greatly enlarged.

AURICULOVENTRICULAR CONDUCTION DEFECTS IN THE PRESENCE OF NORMAL RHYTHM. It has been pointed out that impairment of the passage of the excitation waves

Most Common Symptoms and Signs of Toxicity

In brief summary, the most common toxic manifestations are: loss of appetite, nausea and vomiting; too great slowing of the heart rate, especially in auricular fibrillation; ventricular premature contractions, coupled rhythm; the sudden slowing which indicates complete heart block in either auricular fibrillation or normal rhythm, the sudden halving of the rate in normal rhythm which indicates 2:1 block; an occasional true dropped beat occurring after a pattern indicating partial heart block with Wenckebach phenomenon, a sudden increase in rate suggesting ventricular paroxysmal tachycardia; and prolongation of the P-R conduction time as reflected in electrocardiograms.

Noncardiac Symptoms

DROWSINESS Some patients may become drowsy or complain of headache and malaise when digitalization is accomplished within 24 hours. Drowsiness may be attributed to the fact that the patient is becoming more comfortable and consequently relaxation and rest is possible.

GASTROINTESTINAL SYMPTOMS The most common noncardiac symptom of digitalis intoxication is *loss of appetite*. If under this condition the drug is continued, nausea and vomiting may occur. Further gastrointestinal distress may be prevented by discontinuing the drug One has only to see the distress that these effects cause in a patient who is already sick to be convinced that these toxic manifestations should be avoided Moreover it has been shown that with the onset of nausea and vomiting the cardiac output decreases, and since the output is already lowered in congestive heart failure, it is surely not good practice to lower it further. Sometimes nausea and vomiting may persist so that the patient develops acidosis, with an acetone odor to the breath. When these toxic symptoms result from use of the whole leaf they are likely to be of shorter duration than when digitoxin is used

Nausea and vomiting which occur during digitalization with the whole leaf have been attributed to gastrointestinal irritation; when they occur later it has been attributed to central nervous system toxicity. When the whole leaf is given carefully there is no greater incidence of nausea and vomiting than from the glycosides. Batterman and DeGraff think that if nausea and vomiting result from maintenance doses of digitalis leaf, it is of central origin, and would occur with glycosides if they were given in comparable doses If vomiting persists it may become necessary to give fluid and glucose by hypodermoclysis or even intravenously. Patients usually find that charged beverages such as ginger ale and soda water offer relief.

In my experience diarrhea is of infrequent occurrence with either the whole leaf or the glycosides.

YELLOW VISION. Yellow vision is seen occasionally as a toxic manifestation of digitalization. Green vision and haziness of vision have also been reported In my experience visual disturbances have been infrequent, although I have observed yellow vision in one patient who was receiving digitoxin. A patient has been reported who had complete heart block with restriction of visual fields, in this case the digitalis intoxication disappeared slowly after the drug was discontinued. Wagener, Smith, and Nickeson have reported retrobulbar neuritis with complete

pattern the amplitude of the QRS complexes varies alternately from lower to greater voltage, but their direction remains unchanged and does not alternate.

Ventricular paroxysmal tachycardia is a serious complication of the drug, and *requires that it be discontinued. We have seen patients succumb to the continued* use of digitalis in the presence of ventricular paroxysmal tachycardia. Pronestyl should be used if this rhythm occurs in the course of digitalis therapy (p. 178).

VENTRICULAR FIBRILLATION. Ventricular paroxysmal tachycardia occurring as a result of overdigitalization may itself be fatal, or the rhythm may change to

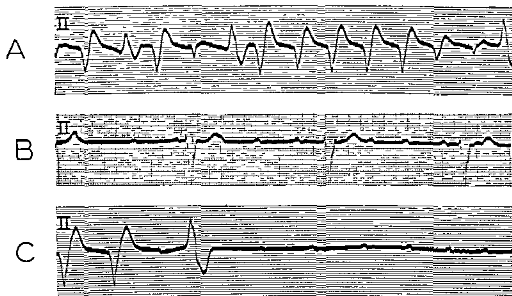


FIG. 19

Ventricular Paroxysmal Tachycardia from Changing Focus in the Two Ventricles Resulting from Digitalis Intoxication. Patient was male, aged 65 years. *A.* Ventricular paroxysmal tachycardia

block with ventricular asystole, auricles continuing to beat at 75 per minute (shown in C). This pattern was repeated until cardiac activity ceased.

ventricular fibrillation. Since persistence of the latter rhythm cannot sustain the circulation, death ensues. Ventricular fibrillation may result also when quinidine is used in the presence of frequent ventricular premature contractions or of ventricular paroxysmal tachycardia due to digitalis.

AURICULOVENTRICULAR RHYTHM. Auriculoventricular rhythm may occur early in digitalization on amounts short of the full therapeutic dose, in which case the digitalis can be continued. But when auriculoventricular rhythm occurs after large amounts of digitalis, the drug should be discontinued.

AURICULAR STANDSTILL. Auricular standstill may occur from overdigitalization.

down the auriculoventricular conducting system from the auricles to the ventricles is one of the significant effects of digitalis. This is recorded in the presence of normal sinus rhythm as prolongation of the auriculoventricular conduction (P-R) time in the electrocardiogram. The usual therapeutic amounts of digitalis do not often significantly alter the P-R time (Fig. 12). Increase in the P-R time beyond the usual expected variations or its prolongation beyond 0.20 second may be one of the early toxic effects of digitalis. The P-R time may remain prolonged. If there is further accumulation of digitalis, partial heart block in which occasional P waves are blocked may result (Fig. 31C). A common pattern is the *Wenckebach phenomenon*, in which gradual increase in P-R occurs until a P wave is blocked On other occasions high grade block may be seen, such as 2:1 or 3:2, in which every other P wave or every third one is blocked. Finally, there may be complete auriculoventricular dissociation or complete heart block (Fig 11). At times the ventricular rate in complete heart block due to digitalis is not slow but may be at a higher rate—60 to 80, or more

Whenever, in the course of digitalis therapy in patients with normal sinus rhythm, "dropped" beats appear which can be detected on physical examination, the onset of partial heart block should be considered and digitalis discontinued When the heart rate suddenly decreases to half its usual rate, 2:1 heart block is a likely diagnosis. When the ventricular rate becomes slow—around 30 per minute—complete heart block is likely to have occurred. It is recalled that the vagal effect of digitalis may give rise to rather marked slowing (Fig. 10) of the rate of sinus discharge so that sinus bradycardia may ensue.

With all except moderate increases in P-R time, digitalis should be discontinued until the conduction defect disappears. These effects persist longer when they are due to digitoxin than when digitalis leaf is the cause.

When organic conduction defects are present as might have resulted from active rheumatic fever or arteriosclerotic changes, digitalis in therapeutic amounts may be given without increasing the degree of heart block

Vagovagal syncope has been reported as a toxic manifestation of digitalis in a patient in whom the carotid sinus was sensitive and in whom there was an esophageal diverticulum. Swallowing or distending the esophagus at the level of the diverticulum with a balloon resulted in Adams-Stokes syndrome when the patient was under the influence of digitalis.

VENTRICULAR PAROXYSMAL TACHYCARDIA *Ventricular paroxysmal tachycardia* may result from overdigitalization. At first frequent ventricular premature contractions may be detected. These increase in number, then become multiple or occur in a sequence of varying lengths, which are in fact short runs of ventricular paroxysmal tachycardia. Finally ventricular paroxysmal tachycardia arising from one or the other ventricle becomes the established rhythm. Occasionally in digitalis intoxication the ventricular paroxysmal tachycardia may be bidirectional (Fig 34F) with alternation of the focus of origin from one ventricle to the other in each successive beat. At other times the site of origin may change from one ventricle to the other without any fixed pattern (Fig 19). Ventricular paroxysmal tachycardia with electrical alternans has been observed after an excessive amount of digitalis. In this

heart muscles. Necrosis of the myocardium is more easily induced by digitalis in older than in younger animals, observations which have just been cited in the foregoing section on the toxic effect on heart muscle.

Toxicity Resulting from Diuresis

Toxicity has been reported in digitalized patients when marked diuresis occurs with mercurial diuretics. This has been attributed to the concentration of digitalis in the body resulting from rapid mobilization of fluids. Nausea, vomiting, and ventricular premature contractions are said to occur. I have not encountered this sequence of events and am not convinced that it occurs. Kissane and Koons, however, were of the opinion that there was reabsorption of digitalis substances from edematous fluids. They thought toxicity was not due to the mercurial diuretics per se since it also occurred following rapid diuresis with glucose. The symptoms they described were nausea and vomiting, headache, weakness, premature contractions, coupling, transient auricular fibrillation, and flutter. The combination of all of these symptoms and signs are so rarely seen after digitalis intoxication that it does not appear to me to be established that they are due to digitalis, since they are compatible with symptoms and signs of sodium or perhaps potassium depletion. Low serum potassium may make cardiac tissue more sensitive to the concentration of digitalis which is available

Eosinophilia

Eosinophilia reaching 30 per cent has been reported as a toxic manifestation of digitalis, but I have not had occasion to see it It is indeed of rare occurrence The effect has been attributed to the vagal action of the drug

OPTIMAL VENTRICULAR RATE IN AURICULAR FIBRILLATION

The ventricular rate in the presence of auricular fibrillation can and should be retarded to the optimal rate since digitalis has a specific effect in slowing it. I have considered a resting ventricular rate of 70 to 75 beats per minute to be the optimal level. In most patients with auricular fibrillation the rate before treatment is usually labile and shows marked fluctuations. When the patient has been adequately digitalized, the fluctuations are usually slight. We have been impressed, however, that this is more likely to be the case when patients have been digitalized with

If the resting ventricular rate is retarded to 70 beats per minute, under moderate exertion it might increase to 90 to 100 beats per minute, and under more marked exertion to 110 to 120 per minute, with appropriate increases for longer and more marked exertion. The range may not be much more than is seen in patients with normal sinus rhythm, with a resting heart rate of 70 per minute. On the other hand, if the resting rate is around 80 to 90 per minute, under moderate exertion the rate increases to 100 to 120 per minute and under greater exertion to higher levels. Since all muscular and metabolic activities require increased volume outputs

I have observed it once in a patient who took 20 to 30 tablets of digitalis of his own accord although he was already digitalized.

AURICULAR FIBRILLATION. The induction of auricular fibrillation by digitalis has been reported. Since patients with many forms of heart disease are prone to have auricular fibrillation, it is difficult on most occasions to attribute the onset of this rhythm to digitalis. This toxic effect must indeed be rare when one takes into account the number of patients with normal rhythm who are digitalized and the expected incidence of the rhythm in the natural history of the particular type of heart disease.

It is recalled that when animals are given *lethal amounts* of digitalis the heart dies in systole and is contracted.

Interference dissociation has been reported from the use of digitalis.

Toxic Effect on Heart Muscle

There have been several papers in the literature concerning the toxic effect of digitalis glycosides on heart muscle. In animals myocardial necrosis as well as fibrosis and atrophy have resulted from giving digitalis leaf, lanatoside A, B, or C, digitoxin, and strophanthin in amounts which are beyond the therapeutic ones. Local spasm of the coronary vessels has been suggested as the cause of these anatomic changes. They appear to be more easily induced by the purified glycosides than by the whole leaf and tincture. They are more readily induced in old hearts than in young ones The electrocardiographic patterns in animals given toxic amounts of the digitalis bodies are different from those recorded when therapeutic amounts are used. With toxicity, negativity and coving of $T_{1,2,3}$ and negativity and coving of $T_{2,3}$ with T_1 upright and abnormalities of the RS-T segments have been described. Electrocardiograms return to the control form if the animals recover. The heart muscle shows scarring in animals which survive.

These observations are cited as a reminder that digitalis should be treated with deep respect, not only with regard to the occasions for its use but also as to its dosage. It is hardly likely, except under unusual circumstances, that it will be given in amounts—in a single dose or cumulatively—that will induce comparable changes in the human heart.

Clotting of the Blood

Several papers have appeared in the last few years suggesting that digitalis favors the tendency to thrombosis. Shortening of the coagulation time and increase in the prothrombin level have been reported. That this drug plays any considerable part in the formation of thrombi in clinical heart disease has not been demonstrated. These theoretical considerations should not interfere with our clinical use of the drug.

Age and Toxicity

It is the general notion that toxic effects on the heart from digitalis are more easily induced in older individuals than in younger ones. Ventricular premature contractions may be more easily induced in old patients with myocardial changes due to coronary artery disease and resulting fibrosis than in patients with younger

TONIC DOSES OF DIGITALIS

"Tonic" doses of digitalis were small amounts, comparable to what are now called maintenance amounts, that were given without previous digitalization. I can see no appreciable benefit in tonic doses, except in the following manner: We know that the ventricular rate in the presence of rapid auricular fibrillation can be retarded after a period of many weeks by giving small amounts of digitalis daily. A certain portion of this small amount is retained for digitalization and a certain portion is excreted. After a long period, enough of the drug is accumulated to slow the ventricular rate to a nearly satisfactory level It may be that tonic doses act in the same manner, namely that there is gradual accumulation to a therapeutic level even though it is not maximal. It is the general opinion of clinicians now that when digitalis is indicated it should be given in the full therapeutic amount

SIMULTANEOUS USE OF QUINIDINE AND DIGITALIS

I do not advise the simultaneous use of quinidine and digitalis The method I use to convert auricular fibrillation and auricular flutter to normal sinus rhythm by the use of quinidine in digitalized patients is discussed on pages 148–149 and 155.

In the treatment of ventricular paroxysmal tachycardia resulting from digitalis it is best not to use quinidine because the tachycardia may be changed to the bidirectional type or to ventricular fibrillation, either of which may be fatal

When quinidine was given to one patient with ventricular paroxysmal tachycardia arising from changing foci (Fig 19A) as a result of digitalis intoxication, there first occurred complete heart block with bundle branch block (Fig 19B), followed by transient runs of ventricular paroxysmal tachycardia from changing foci and then by long periods of ventricular asystole (Fig 19C) During these intervals the auricles continued to beat under the direction of the sinus node With the persistence of these changes in rhythm, death occurred.

I do not recommend the use of quinidine to eliminate ventricular premature contractions in digitalized patients

Procaine amide hydrochloride (pronestyl) appears to be useful in the treatment of ventricular paroxysmal tachycardia and ventricular premature contractions due to digitalis (p. 178)

CHANGE FROM ONE DIGITALIS PREPARATION TO ANOTHER

On many occasions the shift from one preparation of digitalis to another can be made easily, but in others special attention must be given to the different rates of excretion of the two products.

For the most part whole leaf digitalis U S P XIV and digitoxin may be interchanged if it is kept in mi[illegible]
for clinical purposes to 0.1 [illegible]
given either orally or intra[illegible]
administration and in the same amounts as would have been required by the route

of blood from the heart, thus increasing the heart rate, during most of the day the higher levels of the heart rate will prevail.

A more important factor is the *pulse deficit.* When the ventricular rate is 70 beats per minute pulse deficit is absent, negligible, or small. With increase in ventricular rate, however, the pulse deficit increases—in short, there is an increase in the number of beats that are wasted with respect to maintenance of the volume output of blood from its chambers. The physician should be impressed with the wisdom of keeping the ventricular rate slow when he realizes that the heart is spared 115,200 beats in 24 hours by slowing the ventricular rate from 150 per minute to 70 per minute and when he takes account, through the pulse deficit, of the number of wasted beats in this period. The multiplication of this number of wasted beats by days, months, and years reveals a saving which reaches enormous dimensions. The cardiac output per minute may be optimal at around this rate—70 per minute. Moreover it has been shown that the resting cardiac output when failure is present in many patients with organic heart disease—especially those with mitral stenosis—is the most that can be attained. Exercise results in shifting the blood flow from less demanding areas to those requiring more; in this way deficits are accumulated which must later be restored.

Subjective Observations By Patients

Most patients are usually unaware of the beating of the heart when its rate is around 70 per minute If its rate is more rapid they may complain of "throbbing" or "fluttering." When the rate is retarded to around 50 per minute certain patients may complain of forceful, slow beating. A few patients prefer a resting heart rate of 60 to 65 per minute, but usually the optimal resting rate is 70 to 75 per minute. Certain patients, who have been trained to adjust their own digitalis dosage by counting the heart rate, select the level at which they feel best, which varies from the low range to around 70 per minute.

CALCIUM AND DIGITALIS

Certain observations indicate that in the presence of calcium ions digitalis induces premature contractions more readily than when it is used alone (Stewart). Other observations do not indicate an additive or synergistic action Nevertheless, sudden deaths have been reported from the intravenous use of calcium salts in digitalized patients It is therefore strongly recommended that this use of calcium salts be avoided It is best not to use either the macrosal solution which contains calcium salts or calcium gluconate in the measurement of circulation time in digitalized patients since the test substances must be injected too rapidly. Experiments showing the innocuous effects on the heart of digitalis and calcium in animals in which both the myocardium and the coronary arteries are normal, may not be applicable to patients with heart disease in whom the myocardium may be damaged and heart failure may be present. I have recently seen an instance of immediate death following the intravenous injection of calcium gluconate in a digitalized patient.

not be so predictable, should *rarely* be necessary. Lanatoside C or digitoxin may be used by this route when question of absorption of the drug from the gastrointestinal tract arises.

Rectal Digitalization

Levy has shown that digitalization can be accomplished rapidly and safely by giving a soluble digitalis product by rectum. This route was formerly used when digitalis could not be given by mouth For rapid absorption a cleansing enema should be given first. The digitalis is then given as a micro-enema. Formerly, a preparation of digitan was available for rectal use. Because glycosides, which can be given intravenously, are now available when oral digitalization is not possible, the occasions for rectal digitalization should be rare

AMBULATORY DIGITALIZATION

In many instances digitalization can be achieved while the patient remains ambulatory, but under this condition digitalization should be carried out more slowly than when the patient is at rest in bed. Clinic patients and office patients who are not very sick or who have only moderate failure may be suitable for ambulatory digitalization. From the average amount of the preparation required for digitalization in 24 hours, together with the average daily maintenance amount and the number of days it is decided to use for digitalization, one can calculate *the total amount required for digitalization with maintenance in this number of days.*

Whole Leaf

If one week is allotted to digitalization, then 1 8 Gm digitalis leaf (U S.P. XIV) to digitalize *plus* 0 9 Gm to maintain digitalization (0 1 Gm alternating with 0 2 Gm. for six days rather than 0 2 Gm. daily) *amounts to* 2 7 Gm. to be given

Table III. Ambulatory Digitalization Over a Period of One Week

Day	*Digitalis (U.S P XIV)* A M		P M		*Amount for the Day*	*Total to Date*
1	0 3 Gm	+	0 3 Gm	=	0 6 Gm	0 6 Gm.
2	0 3 Gm	+	0 2 Gm	=	0 5 Gm.	1.1 Gm.
3	0 2 Gm	+	0 2 Gm	=	0 4 Gm	1.5 Gm.
4	0 2 Gm	+	0 1 Gm	=	0 3 Gm	1.8 Gm.
5	0 2 Gm	+	0.1 Gm.	=	0 3 Gm.	2 1 Gm.
6	0 2 Gm	+	0 1 Gm	=	0 3 Gm	2 4 Gm
7	0 2 Gm	+	0 1 Gm	=	0 3 Gm	2.7 Gm

during the week This may be distributed according to the regimen shown in Table III. If the clinical potency of the preparation is not known, smaller amounts are given than those recorded in the table.

Early in the week, when toxic symptoms are not likely to occur, larger amounts

being used earlier. The greatest difficulty is encountered when the *rapidly acting glycosides*, which are also rapidly excreted, are to be replaced by the more commonly used oral or intravenous preparations. When the decision is made, after digitalization, to change over to the whole leaf or, for example, digitoxin, it is not enough to carry on with maintenance amounts. The patient must be redigitalized carefully with increasing amounts of the substituted preparation so that as the concentration of one preparation diminishes, the concentration of the other is increased. In this way, by the time one of the substances is completely dissipated, digitalization with the second preparation is accomplished. This requires care in avoiding toxicity It cannot be done so accurately that the rapid excretion of the one can be made up by the addition of the exact amount, at the right time, of the slower acting, less rapidly excreted preparation. There may be an interval when digitalization is not at the maximal therapeutic level. This lag, however, must be accepted in order not to run into toxic effects

ROUTES OF ADMINISTRATION

Oral Digitalization

In most instances digitalization can be carried out rapidly, effectively, and satisfactorily by the oral administration of the whole leaf or of certain of the digitalis glycosides. The effects from the whole leaf given orally can be seen within one hour and is evident about as rapidly as are the effects of digitoxin by the same route With both of these, digitalization can be accomplished within 18 to 24 hours by the oral route Batterman and DeGraff think that digoxin finds usefulness for the rapid oral digitalization of patients with congestive heart failure.

Intravenous Digitalization

The advantage of digitoxin over the whole leaf is that it can be given intravenously if necessary But there should be no occasion for using digitoxin intravenously when it can be given by mouth In the presence of nausea and vomiting, if digitalis is required after operations, and if its absorption when administered orally is questionable, digitalization may be accomplished by intravenous digitoxin. The speed at which it is safe to digitalize patients with digitoxin intravenously has been already discussed, its effects by this route appear only slightly earlier than when given orally, *and on occasion may not be any more rapid than under digitalization* with the whole leaf by mouth. Maintenance amounts should be given by mouth as soon as possible after intravenous digitalization, just as in the case when maintenance amounts are given transiently by the intravenous route. When an intravenous digitalis preparation is required I prefer lanatoside C.

When rapid digitalization is necessary ouabain or lanatoside C may be used intravenously.

Intramuscular Digitalization

the
may

I have had no experience with children below three and one-half years of age, or with infants, in situations wherein the dosages could be compared with those for the adults. Digitalis is rarely needed in infants, although there are instances reported of paroxysmal tachycardias which have been terminated by small amounts of digitalis given intravenously In infants several days to several months of age, 0 1 to 0 3 Gm of digitalis leaf may terminate attacks of paroxysmal tachycardia. These amounts of the whole leaf or comparable doses of digitoxin or lanatoside C would be used in treatment of heart failure, such as occurs in Kugel's myocarditis

DIGITALIS IN PREGNANCY AND LACTATION

When digitalis is required during pregnancy it is used as in other patients I have not observed, nor am I aware of, any reports of harmful effects of digitalis on the fetus.

There is no evidence that digitalis is excreted in the mother's milk

DIGITALIS IN SURGERY

Patients with heart disease, even those with chronic congestive heart failure, tolerate operative procedures very well, provided adequate attention is given to preparation before operation, choice of anesthesia, skillful surgery, and careful postoperative supervision Indeed in appropriate circumstances the proper use of digitalis may be life-saving for surgical patients The surgeon should therefore be familiar with the circumstances in which digitalis is indicated, and with preparations to use and their correct dosages, or should work with an internist who has supervised such problems The concurrent surgical condition does not change the usual dosage for any therapeutic objective

Normal Hearts

Patients with normal hearts should not be routinely digitalized before operation even when they are in the age group in which cardiac complications may arise.

Diseased Hearts

Patients with heart disease should not be routinely digitalized before operation unless heart failure or abnormality of rhythm may indicate it In patients with normal hearts and those with heart disease before the onset of failure, digitalis decreases the cardiac output and makes the heart too small, both of which may be handicaps under the stress of anesthesia and of the operative and postoperative requirements

Auricular Fibrillation

Patients with auricular fibrillation, whatever the cause, should be digitalized before operation and the ventricular rate retarded to the optimal level If there is time, the drug can be given orally If operation is necessary at once, a rapidly acting drug such as ouabain or lanatoside C can be given intravenously. Even if the

are given. Toward the end of the week, as full therapeutic digitalization is approached, the amounts are decreased. The digitalis schedule shown in Table III is written out for the patient who is warned of toxic symptoms Patients are usually examined again in the middle of the week of digitalization to be certain the schedule is being maintained and that there are no toxic symptoms. Patients record any deviation from the dosage which has been planned For example, if nausea occurs the subsequent doses are omitted until it abates; the schedule is then resumed at the point where it was discontinued.

At the end of the week on the above schedule the patient should be in the range of therapeutic digitalization If auricular fibrillation is present, additional amounts can be given in the next few days should the ventricular rate not have been adequately slowed (that is to 70 beats per minute). If normal sinus rhythm is present, the patient may be considered digitalized since the rate does not serve as a guide After digitalization, maintenance amounts are continued, either 0 1 Gm alternating with 0 2 Gm daily, or 0 2 Gm daily being commonly required. In the case of patients with auricular fibrillation, the amount is given which is found to keep the resting ventricular rate at the optimal level.

Digitalization of ambulatory patients with small daily doses of 0 2 to 0 3 Gm of digitalis leaf requires too long a time for a beneficial effect to appear. This method is *therefore not recommended*

GLYCOSIDES

Ambulatory digitalization with *digitoxin* can be carried out on the same schedule as that given in Table III for the whole leaf. If 1 8 mg is accepted for digitalization and 0 1 mg alternating with 0 2 mg. a day for maintenance, milligrams can be substituted for grams in the program for digitalization given in the table

If the patient can have some supervision and can be seen by the physician at home it may be expedient for digitalization to be carried out within 24 hours while the patient remains in bed In certain other instances *lanatoside* C or *digoxin* may be used for rapid digitalization while the patient remains in bed for the day of digitalization.

DOSAGE OF DIGITALIS IN CHILDREN

The average *amount of digitalis required to bring about optimal therapeutic* effects is approximately the same *regardless of body weight and of age* (Figs. 5 and 6). The discrepancy between the amount actually required for digitalization in children and the amount derived when it is calculated on the basis of body weight shows the futility of calculating digitalis dosage according to body weight. Extensive studies, similar to those for adults, have not been carried out relating to the amount of digitalis required for adequate digitalization of children exhibiting auricular fibrillation with a rapid ventricular rate I have seen patients with rapid auricular fibrillation as young as three and one-half years, yet they required the same amount of digitalis to slow the ventricular rate as do adult patients I have proceeded on the concept that it requires approximately the same amount. When digitalis is given slowly and in the broken doses, intoxication need not occur.

DIGITALIZATION IN ANGINA PECTORIS

Digitalis should not be used in the treatment of angina pectoris unless there is also heart failure or other definite indication for the drug In the absence of heart failure, digitalis may decrease the cardiac output. As a consequence a decreased amount of blood will be available to the coronary vessels, and angina may be aggravated. In fact, when digitalis was given to one normal subject, angina was experienced on exertion when the decrease in cardiac output and heart size was at its greatest. This was attributed to decrease in blood flow to the coronary arteries. Clinical experience shows that in the absence of heart failure digitalis does not provide any relief from angina, on the other hand, with the onset of heart failure angina may disappear or lessen, just as it does occasionally with the onset of auricular fibrillation

DIGITALIZATION IN PNEUMONIA

Twenty to twenty-five years ago it was almost a routine procedure to digitalize patients suffering from lobar pneumonia but this practice has been discontinued With the introduction of antibiotics in the treatment of pneumonia the mortality rate has declined and the clinical course of the disease has been altered so that complicating cardiac irregularities—auricular fibrillation and auricular flutter—are infrequent The indications for digitalis in pneumonia are heart failure and appropriate abnormalities of rhythm Since rapidly acting digitalis preparations are available a digitalis effect can be achieved quickly when necessary

DIGITALIZATION IN HYPERTHYROIDISM

The use of digitalis in hyperthyroidism with heart failure, with normal rhythm, with auricular fibrillation, and with auricular flutter is discussed in Chapter 14

SUMMARY

Digitalis is one of the most important drugs at the command of the physician There is no other drug at present which can satisfactorily replace it for the purposes for which it is intended Advances have been made in the isolation and preparation of the active principles of digitalis In most instances the whole leaf preparation serves a good purpose in both digitalization and the maintenance of digitalization Still the physician should have available a preparation which can be given intravenously for occasions when the use of the oral preparation is not feasible and when rapid effects are required The various glycosides induce their effects at different speeds and also have different rates of excretion, so that each may come to have more or less special areas of application

Digitalis has definite indications for its use, as well as definite contraindications If experience is gained with the preparations commonly employed, certain results may be expected from the preparation at given stages of digitalization, and on

ventricular rate is slow, it is best to digitalize the patient to prevent its rising beyond bounds with anesthesia and the operative manipulation.

Restoration of Compensation Prior to Surgery

Patients with heart failure should be digitalized before operation, together with whatever other measures are indicated to restore compensation. If the operative procedure can be delayed until the patient has been restored to compensation, the outlook is better. Should delay be impossible, rapid digitalization should be instituted by using ouabain or lanatoside C

Acute Failure During Operation

When patients develop acute heart failure during operation, rapid digitalization by an intravenous preparation should be carried out at once. Ouabain or lanatoside C may be used. If cardiac failure occurs postoperatively, digitalization can be accomplished rapidly by the oral route, or intravenously if it is more urgent Additional measures are used as indicated. aminophyllin intravenously, oxygen, and a mercurial diuretic.

It is, however, much better to avoid factors which precipitate heart failure during operation or postoperatively. One of the major causes of heart failure is the *administration of too large amounts of fluid intravenously.* This is also a common cause of acute cor pulmonale in surgical patients. Patients with heart disease who have never had failure, as well as patients with a history of heart failure who are compensated with or without cardiac medication at the time of operation, or even patients without any apparent heart disease—all these require careful observation The anesthesia, the operative procedure, and large amounts of intravenous fluids may all add up to more than the cardiovascular system can tolerate. The use of intravenous fluids may not be necessary in certain patients with heart disease; fluids may be given subcutaneously by hypodermoclysis. *Hyaluronidase* added to the solution facilitates absorption The oral route should be substituted for hypodermoclysis and intravenous fluids as soon as possible. Observation of the state of the neck veins, râles at the lung bases, and cyanosis should be made frequently during infusions. The amount of fluid which is introduced into the circulation should take into account the amount of sodium added to the body. Neither sodium bicarbonate nor one-sixth molar sodium lactate should be used to prevent crystalluria when sulfonamides are used As soon as possible cardiac patients should be restored to their regular cardiac regimens of reduced fluid intake and restriction of salt. During the postoperative course continued use of mercurial diuretics may be required when giving fluids intravenously Pulmonary infarction, bronchopneumonia, or a bout of paroxysmal tachycardia postoperatively may precipitate heart failure.

Paroxysmal Rhythms

Paroxysmal rhythms should be terminated as quickly as possible by the drug likely to have the most rapid effect and, if possible, by one which does not preclude the use of other drugs if the first is not effective. Digitalis is contraindicated only if the rhythm is that of ventricular paroxysmal tachycardia.

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most occasions this drug will not disappoint. Digitalis should be given in adequate amounts to secure maximal therapeutic effects without toxicity; when a continued effect is required, the amount which is excreted should be matched by a daily ration amount Digitalis alone may be of sufficient benefit in the treatment of heart failure without the use of other drugs, at other times the addition of other diuretics is necessary Since heart failure arises because of the inability of the heart to maintain an adequate circulation, whatever the mechanism by which edema occurs, I think that heart failure is more satisfactorily treated with digitalis—a drug favorably influencing the action of the heart—together with whatever additional measures are required, rather than by the use of mercurial diuretics alone. It is well to remember that digitalis still remains an effective drug for the treatment of the condition for which Withering introduced it, namely dropsy.

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CHAPTER 4

Anticoagulant Drugs

INTRODUCTION

Historical Background

A considerable literature has appeared in recent years relating to the use of anticoagulant drugs in the treatment of intravascular and intracardiac clots For some years anticoagulants have been used in the treatment of thrombophlebitis and pulmonary infarction due to thromboembolism Solandt, Nassim, and Best in 1938 and 1939 suggested the use of *heparin*, a substance discovered by McLean in 1916. In 1940 and 1941 Link and his associates described a second anticoagulant, *dicumarol* [3.3 methylene-bis (4 hydroxycoumarin)]. This substance was first isolated from spoiled sweet clover, the ingestion of which by cows resulted in a hemorrhagic disease. Later dicumarol was synthetized from coal tar compounds

Gauging of Effects

The exact mechanisms by which heparin and dicumarol induce their effects on the blood are not yet precisely known. The effect of heparin is measured in terms of its prolongation of the *coagulation time* of the blood, the effect of dicumarol is gauged in terms of its prolongation of the *prothrombin time* of the blood. The action of heparin is apparent within a matter of minutes after injection into the blood stream. Dicumarol, a drug which must be given orally, is slower in its action, 48 to 72 hours being required for its full effects to be manifested, so that the patient is not fully protected in the early hours of its administration. The changes resulting from heparin are dissipated within a matter of hours, while those of dicumarol are prolonged over several days. When these drugs are used it is imperative that samples of blood should be examined frequently enough to gauge their effects

Anticoagulants should not be used unless a competent laboratory staff is available

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prolonged shortly after the injection, then falling before the next injection. Attempts are made to gauge the amount of heparin and the time interval so that the clotting time never drops below 15 minutes.

A variant of the intermittent intravenous method which has been found to work effectively is as follows. After measurement of the clotting time, 50 mg. of heparin is given intravenously The clotting time is estimated one-half hour, two hours, and three hours afterward. Heparin is then given intravenously at six-hour intervals. Each dose is increased or decreased according to the response to the previous injection. The amount most frequently required to keep the clotting time at the optimal level is approximately 50 mg. every six hours The dose is seldom less than 35 mg. or more than 75 mg. After the pattern of response to the first dose is plotted, the clotting time need be estimated only once daily, before one of the injections In the hospital on this schedule, the regimen can be planned so that an injection is given at midnight, and another would come due at 6 A.M. According to wide experience in Sweden, it apparently does not affect the clinical course adversely if the clotting time returns to normal by the time the next injection is due

It might be emphasized that the administration of heparin by the intravenous method is a form of treatment that can be carried out easily, and the estimation of its effect on clotting time is readily observed, requiring no special laboratory facilities. It is safer to use than dicumarol in most places where the laboratory technic of estimating prothrombin time is uncertain It would be used more extensively were it not for the excessive cost and the inconvenience of intravenous administration.

Intermittent Subcutaneous Route

Cosgriff has used the following schedule One-half hour after an initial intravenous injection of 25 mg of the sodium salt of heparin. 50 mg. is given in the deep subcutaneous tissues, and beginning three hours later 30 mg. is injected subcutaneously every three hours This method provides for a more even level of the clotting time than does the intermittent intravenous schedule

Table IV. Depo-Heparin Sodium
(Contents per cubic centimeter)

Heparin sodium (20,000 units)	200 mg
Gelatin	180 mg.
Dextrose	80 mg

Preserved with sodium ethyl mercurithiosalicylate 1 10,000

A commercial preparation of sodium heparin, "Depo-Heparin"* is available for subcutaneous or intramuscular use The initial dose may be 200 mg Clotting time is measured before injection and at six-hour intervals The sodium salt of heparin is dissolved in gelatin so that its absorption will be retarded (Table IV). Consequently the effect on delaying clotting time will not occur abruptly and will not be marked, but it will be prolonged.

* The Upjohn Co.

to make the appropriate blood tests at required intervals The laboratory technician should be familiar with the coagulation time and prothrombin time technics and with the sources of error which may arise. *The times are not reliable* unless they are done regularly.

Contraindications

These drugs are contraindicated in the following conditions: blood dyscrasias with bleeding tendencies, polycythemia vera, serious liver disease, serious renal disease, especially with hematuria or renal calculi, subacute bacterial endocarditis, gastrointestinal lesions such as gastric ulcer, ulcerative colitis, or diverticulitis which might be the source of hemorrhages; tumors of the gastrointestinal tract, recent hemorrhage, especially in the brain; severe hypertension, especially if there is a history of cerebral accidents; recent threatened abortion, the final stages of pregnancy; and finally, in the early postoperative period, especially after operations upon the central nervous system.

Combined Use

Since heparin acts rapidly it is common practice, if dicumarol is to be used, to give heparin to achieve an immediate effect and to continue its use for 36 to 48 hours until the dicumarol, which has been started at the same time, has become effective

HEPARIN

Heparin may be given in four ways (1) by the intermittent intravenous method, (2) by the intermittent subcutaneous method; (3) by the continuous intravenous method, (4) by the intermittent intramuscular method; and (5) by the sublingual route

Intermittent Intravenous Method

Estimation of the coagulation time beforehand should reveal a value between five and eight minutes according to the Lee-White technic. The average normal time is six and one-half minutes. If it is planned to replace heparin by dicumarol later the prothrombin time should be recorded also. An intravenous injection of 50 mg of heparin is then given slowly, either diluted in 50 to 100 cc of normal saline or undiluted Clotting times are recorded 15 minutes and two and one-half hours later. If the clotting time at the two and one-half hour reading is less than 15 minutes, 75-mg amounts of heparin are given for the subsequent doses After the first few doses have been given the pattern of the clotting time is available so that afterward it may be necessary to estimate the clotting time only once a day before injection of the drug. Usually 50 to 75 mg. at three- to four-hour intervals are adequate to keep the clotting time in the optimal range between 20 and 40 minutes (Cosgriff). The clotting time is measured by the Lee-White modification of the Howell method, which has been briefly summarized by Marple and Wright.

By this method of administration the clotting time varies widely, being greatly

and may cause temperature rise, patients frequently refuse to allow the treatment to be continued. As a consequence this method has not been widely adopted.

The ingredients of the Pitkin menstruum are gelatine 15 to 30 per cent, dextrose 5 to 12 per cent, glacial acetic acid 0.5 per cent, and enough distilled water to make 100 per cent (Table V). Because the material contains gelatin it must be warmed in order to liquefy it before it can be drawn into the syringe for injection. This preparation is said to be suitable for subcutaneous or intramuscular use. It is dispensed in 2-cc. and 3-cc. ampules containing 200 and 300 mg. of heparin respectively and each of these is supplied with and without vasoconstrictors. Loewe advises its use on a body weight program, 300 mg. being required for a patient weighing 150 pounds. He states that if the normal coagulation time by the Lee-White modification of the Howell method ranges from nine to fifteen minutes, a coagulation time of 30 to 60 minutes is considered an adequate heparin effect. He thinks that approximately 90 per cent of the subjects require 300 mg. of heparin and the other 10 per cent either 200 or 400 mg amounts Loewe states that one 3-cc. ampule is adequate to keep a patient heparinized for about two days; the coagulation time, however, is estimated daily. Obviously the preparation containing the vasoconstrictor drugs should not be used in hypertensive patients or in those with myocardial disease.

Depo-Heparin (see p. 105) can be given intramuscularly.

Treatment of Excessive Prolongation of Clotting Time Due to Heparin

The most important toxic effect of heparin to be on the alert for is bleeding. When heparin produces bleeding the drug is discontinued Transfusion of whole blood or relatively fresh bank blood may be given in amounts to replace the lost blood, or to inactivate any circulating heparin in order to restore the clotting time to normal *Protamine sulfate* given as 1 to 2 per cent solution in 50- to 100-mg. doses intravenously returns the clotting time to normal within five minutes. One milligram of heparin is said to be neutralized by 1 to 2 mg. of protamine solution. If protamine should be required too great care cannot be exercised to avoid overdosage since the blood may clot in the body.

Sublingual Heparin

Due to the disadvantages of the other routes of administration of heparin, observations have been made recently on the use of sodium heparin sublingually. Absorption is said to be complete in ten minutes, and the coagulation time of the blood to be consistently prolonged to therapeutically effective levels for four hours (Litwins *et al.*) McDevitt, Huebner, and Wright were unable to confirm these observations.

DICUMAROL

Effect on Prothrombin Time

The estimation of prothrombin time, by which the effects of dicumarol are gauged, is handicapped by two main difficulties First, the laboratory procedures are subject to errors which are difficult both to control and to estimate. Second,

Cosgriff has also given the sodium salt of heparin by intermittent subcutaneous injection at intervals planned to obtain elevation of the venous clotting time for a portion of the period between injections. The drug can be administered without hospitalization, without frequent venipunctures, and without frequent estimations of clotting time. This is a modification of the Swedish plan, which is based on the premise that continuous elevation of the clotting time is not necessary to prevent thrombus formation.

Continuous Intravenous Drip Method

Heparin has been given in 5 per cent glucose or normal saline by intravenous drip. The speed of the infusion is adjusted so that the clotting time is maintained at between 20 to 40 minutes. At the start it may be planned to give 300 mg. of heparin in 24 hours in 1000 cc. of 5 per cent glucose in water. At first it may be allowed to flow at the rate of 25 drops per minute The clotting time should be measured every two hours and the speed of the infusion altered according to the response. The average speed of injection which is required to prolong the clotting time to the optimal level is 20 to 25 drops per minute. The same precautions are usually maintained as during any other continuous intravenous medication, with respect to the patency of the needle and moderate immobility of the extremity, to be certain that the needle does not become dislodged. Plastic catheters have been devised which are more satisfactory than needles.

Intermittent Intramuscular Method

The intermittent intravenous technic requires frequent injections and the clotting time undergoes fluctuations On the other hand the continuous intravenous drip, which avoids these two objections, has two drawbacks of its own: it requires the patient to lie very quiet for the entire period that it is used, and the clotting time must be estimated frequently.

Table V. Heparin/Pitkin Menstruum Formulas

	With vasoconstrictors		*Without vasoconstrictors*	
Heparin, sodium salt, mg	300 0	200 0	300 0	200 0
Ephinephrine hydrochloride, mg	1 0	1 0	0	0
Ephedrine sulfate, mg.	25 0	25 0	0	0
Chlorobutanol, mg	0.5	0 5	0 5	0 5
Eucupin dihydrochloride, mg	1.0	1 0	1.0	1 0
Pitkin menstruum, cc	3 0	2 0	3 0	2 0

The intramuscular route was designed to eliminate the objections to the intravenous route by providing for continuous absorption. The heparin is added to a substance which will delay its absorption. The *Pitkin menstruum* is one preparation used for this purpose, but because it causes painful swellings at the site of injection

opinion that fluctuations may be abolished if patients drink one quart of milk daily.

It should be borne in mind that up to one week may be required for restoration of normal prothrombin activity after the use of dicumarol has been discontinued

Patients should not be allowed to use alcoholic beverages while taking dicumarol since it alters the effect of the drug on the blood.

In female patients the required dosage of dicumarol may vary during menses Most patients require the same amount of the drug; a few require more. If patients bleed excessively during menses on their regular dosage, examinations should be made to ascertain whether it is due to dicumarol or to some other cause, such as fibroma of the uterus.

Duration of Therapy

In most patients dicumarol is administered for three to four weeks after the occurrence of the last thrombosis or embolism (see p. 114).

Treatment of Prolongation of Prothrombin Time and of Hemorrhage Due to Dicumarol

If the prothrombin time rises above 60 seconds, if blood appears in stools or urine, or if there are hemorrhages into skin or mucous membranes, dicumarol is discontinued and *vitamin K* 60 to 72 mg is given intravenously at once and repeated in four hours Synthetic vitamin K, menadione sodium bisulfite, may be given intravenously. Seventy-two milligrams are given if the prothrombin time is moderately excessive, between 60 and 80 seconds If it is over 80 seconds, a second dose of 72 mg is given four hours later. If hemorrhages occur while the prothrombin level is low, 50 mg may be adequate. If hemorrhages are large, transfusions may be necessary

Care should be exercised that intravascular clotting does not occur One of these preparations will usually reduce the prothrombin time to bounds within 12 to 24 hours If normal values are not restored *transfusions of whole fresh citrated blood* in 300- to 500-cc amounts will be effective One or two transfusions may be required

Dicumarol in Ambulatory Patients

Dicumarol should be used in ambulatory patients only if three conditions can be satisfied. (1) the prothrombin time can be measured at frequent intervals (see p 110), (2) the patient can be adequately impressed with the dangers (namely of hemorrhages) which are implied in the treatment so that complete cooperation is assured, and (3) the patient will not be unduly introspective about the close supervision which is required

While patients are under treatment in the hospital, the physician assumes the burden and does not acquaint the patient with the dangers, when the drug is given to an ambulatory patient, the patient must be told what toxic symptoms to watch for and the complications which may arise should he fail to cooperate.

Dosage

If hospitalized patients are receiving dicumarol and the use of the drug on an ambulatory basis is decided upon, the dosage is reduced so that the prothrombin

there is disagreement on the best way to record the results of these laboratory procedures. In many clinics and in the New York Hospital the prothrombin time is recorded, in other clinics, especially the Mayo Clinic, the result is recorded as a percentage of normal prothrombin time. If the latter method could be standardized it would provide for correction should thromboplastin of various strengths be used in carrying out the tests. A curve is plotted of the prothrombin time for various levels of prothrombin activity. The curve for each laboratory has to be plotted. Normal 100 per cent activity (for whole plasma) may be around 14 (±2) seconds; an elevation to 22 seconds would correspond to 30 per cent of normal prothrombin activity, and 45 seconds would correspond to 10 per cent of normal prothrombin activity. Effort is made to keep the prothrombin concentration between 10 and 30 per cent of normal.

The so-called "diluted" prothrombin time (12.5 per cent diluted plasma) is from 35 to 42 seconds. Some observers think that the diluted plasma prothrombin time is more sensitive and therefore a safer guide to therapy than estimation based on the whole plasma. On the other hand the errors in the technic of prothrombin estimations may be exaggerated in the dilution technic The aim should be to keep the "undiluted" prothrombin time between 30 and 50 seconds in order to achieve the maximum effect without toxicity

The prothrombin time should be estimated and found normal before dicumarol is administered. The technics of the *Link-Shapiro method* and the *Quick method* have been recently summarized by Marple and Wright.

Dosage

If there are no contraindications 300 mg is given in a single dose. The prothrombin time is then estimated daily each morning as the basis for the next dose. One hundred to 200 mg is given daily until the prothrombin time reaches 30 seconds, then 100 mg. daily until a time of 35 seconds or more is recorded. When this level is reached dicumarol is not given on that day, and none is given until it has fallen to 30 seconds, when 100 to 200 mg is again given until the time has increased to 35 seconds or more In brief, 100 to 200 mg. of dicumarol is given on each day the prothrombin time falls below 30 seconds, and is withheld on each day it exceeds 35 seconds The aim is to regulate the dosage so that the prothrombin time remains between 30 and 50 seconds In some instances the adequate dosage of dicumarol may be as little as 50 mg, but 50 to 100 mg. is usually required.

Marple and Wright recommend the following schedule for dicumarol which is in common use at the New York Hospital· 300 mg. is given on the first day; on the second and succeeding days if the prothrombin level is less than 30 seconds (equivalent to prothrombin activity greater than 20 per cent), 100 to 200 mg. is administered. If between 30 and 35 seconds (equivalent to prothrombin activity of between 15 and 20 per cent), 50 to 100 mg, if between 35 and 40 seconds (equivalent to prothrombin activity of between 10 and 15 per cent), 50 mg or less, and if more than 40 seconds (prothrombin activity less than 10 per cent of normal) none is given on that day.

Certain patients show marked fluctuations in prothrombin time so that there is difficulty in maintaining satisfactory levels. Swedish investigators are of the

The dosage of tromexan has not been definitely established. It appears from the experience so far accumulated by Burke and Wright as well as by others that a satisfactory therapeutic level of hypoprothrombinemia may be secured by an initial dose of 1500 mg. followed by single daily doses of 600 to 2400 mg, or a dose of 300 to 900 mg two or three times a day

ANTICOAGULANT No. 63

4-Hydroxycoumarin anticoagulant No 63 (2-methyl-2-methoxy-4-phenyl-5-oxodihydropyrano-[3,2-c] [1] benzopyran) has anticoagulant properties and has been given clinical trial in a few patients by Hanson, Barker, and Mann.

The prothrombin time was in the therapeutic range in 24 to 96 hours after administration of this drug, the greater number being in 48 hours. Its action persists longer than dicumarol, on the average 8 days The doses of the drug to induce therapeutic hypoprothrombinemia, as were the amounts to maintain the effect, are roughly one-half to one-third the amount of dicumarol in milligrams. These authors thought it somewhat more dependable than dicumarol and that maintenance with it was more readily accomplished. Vitamin K_1 in 500-mg. doses, given orally or intravenously, is effective in accelerating the return of the prothrombin time to normal after it has been prolonged by anticoagulant No 63. On the other hand menadione sodium bisulfite in doses of 72 mg. may reduce the excessively prolonged prothrombin time to the therapeutic range, but has only a slight effect in accelerating its restoration to normal.

COMBINED USE OF HEPARIN AND DICUMAROL

If heparin is used to provide prolongation of the clotting time while dicumarol —which has been started at the same time—is taking effect, the two drugs are given as described for each of them alone The prothrombin time as well as clotting time is estimated before each dose of heparin (when given intermittently), since large amounts of heparin in the blood may affect the prothrombin activity. When heparin is given continuously by drip the rate of flow is slowed before drawing blood for the test. Heparin being given by intravenous drip may be discontinued after 24 to 48 hours. Four hours after stopping the heparin the prothrombin level should be estimated and the dosage of dicumarol for the day decided upon. From then on the regimen is the same as described under the use of dicumarol alone.

Should the prothrombin time fall to 30 seconds, indicating reduction of prothrombin activity to 20 per cent of normal—usually between 24 and 36 hours after the first dose of dicumarol—the heparin is discontinued

The most common regimen at present is the subcutaneous injection of 200 mg. of heparin in a slowly absorbed preparation such as Depo-Heparin At the same time 200 to 300 mg of *dicumarol* is given *orally* In the next 24 hours if examinations of the blood show that optimal levels of clotting time and prothrombin time are attained, further heparin is not given. If the prothrombin time has not attained the optimal level and the estimation of the clotting time warrants it, further amounts of heparin are given subcutaneously. The schedule for dicumarol is given on p. 108.

time maintains a level of between 25 and 30 seconds. The amount required varie from patient to patient; as low as 50 mg. daily may be adequate, while in othe patients the total dosage per week ranges between 400 mg. and 900 mg. While th patient's response to the drug is being observed daily estimations of prothrombi time are necessary. After the pattern has been established, measurement o prothrombin time may be necessary only once or twice a week. If the drug i started in an ambulatory patient it is best to make daily estimations of th prothrombin time until the pattern of the changes in prothrombin time is known

In view of the importance of daily estimations of prothrombin time as the basi for the dosage of the drug, it seems paradoxical that dicumarol should be given t ambulatory patients with prothrombin times estimated as infrequently as onc a week.

In addition to the therapeutic indications for the use of dicumarol in ambulator patients certain factors must be taken into consideration in deciding to prescrib the regimen for the patient: Has the patient the emotional stability to adapt t the exacting schedule which must be maintained; can the patient be depende upon to adhere to the regimen; can the requirement about abstinence from th use of alcohol be met.

OTHER ANTICOAGULANTS

Paritol

Since heparin is expensive and its effect of short duration, search has been made for a drug having its properties but which is free of these two drawbacks. Studies are being made on Paritol, a sulfuric acid ester of polyanhydromannuronic acid. This is a quick-acting anticoagulant drug producing a significant prolongation of the clotting time when given intravenously. For equal doses the effect of Paritol upon maximum clotting time is approximately one-seventh that of heparin. Its action is maintained for eight to twelve hours as compared with the four to five hours of intravenous heparin Paritol has been used effectively for as long as eight days by Wright and his associates. Its use is not free from reactions The place of this anticoagulant has not yet been finally established

Tromexan

A recently introduced coumarin derivative, 3,3'-carboxymethylenebis (4-hydroxycoumarin) ethyl ester, produces a significant prolongation in the prothrombin time. It may find some application in place of dicumarol because of its faster absorption and utilization Hypoprothrombinemia occurs 18 to 24 hours after the initial dose and has reached its maximal level in 30 hours—while 48 to 72 hours may be required for definite dicumarol effect to be apparent, with return to normal 48 to 60 hours after a single initial dose In short the duration of the anticoagulant effect is about one-half to one-fourth that of dicumarol It has approximately one-fifth the potency of dicumarol. For these reasons tromexan may be suitable only for hospital use while dicumarol lends itself to use in ambulatory patients.

pressure. If it turned out that there were more women and more patients with hypertension in the control group than in the treated group, the statistics would be weighted against the control group. These factors will be considered in detail in the final report of the committee.

Russek, Zohman, White, and Doerner have analyzed the risk to patients treated by conservative methods for a first attack of acute myocardial infarction without the advent of serious signs or symptoms within the first 24 hours of hospitalization. The mortality rate was 2 45 per cent and the incidence of thromboembolism was less than 1 per cent. Making allowances for the deaths which were not preventable by anticoagulants, the theoretical preventable deaths in this group was less than 1 per cent. They concluded that dicumarol therapy should not be used routinely in the treatment of all patients with acute myocardial infarction.

RESULTS OF OTHER STUDIES Individual series of patients treated with dicumarol have been reported by Nichol and Page in 1946, Peters, Guyther, and Brambel in 1946, Parker and Barker in 1947, Glueck, Strauss, Pearson, and McGuire in 1948, Greisman and Marcus in 1948, and McCall in 1948. In all of these reports the authors concluded that anticoagulant therapy altered the mortality rate favorably to a significant degree and reduced the incidence of thromboembolic phenomena

AUTHOR'S OBSERVATIONS AND RECOMMENDATIONS At the New York Hospital (where patients with myocardial infarction due to coronary thrombosis have been treated according to an established routine for the last seventeen years) the high mortality rate recorded in the statistics now being reported have not obtained for the patients whom I have personally observed and whose treatment has been under my direct supervision Neither has the control untreated series at the New York Hospital in this cooperative study shown the high mortality rates recorded in some clinics, nor does the comparison between the treated and untreated groups show such a marked difference with respect to mortality and to thromboembolic phenomenon I do not agree that anticoagulants should be given to every patient with myocardial infarction resulting from coronary thrombosis, although it is possible that further investigations or the development of new anticoagulants may alter this point of view. I have recently seen the occlusion of a coronary artery with re-

been inappropriate to have done so While the most common cause of myocardial infarction is coronary thrombosis, the internal or medial hemorrhage just described is frequent enough to make one hesitate to use anticoagulants without consideration of the risk which may be involved

My recommendations and my present practice in the use of anticoagulants are as follows

1 Anticoagulants are not used if the patient, when first seen, appears from the symptoms and from the history to have a small and not severe lesion. This is especially applicable when it is a first attack

2 Anticoagulants are not used in patients with severe myocardial infarction—especially if it is the first attack—who have no evidence of such complications as arrhythmias or heart failure, and in the absence of thrombotic complications.

3 Anticoagulants are used immediately in severe myocardial infarction if heart

CLINICAL APPLICATIONS

Coronary Thrombosis with Myocardial Infarction

Observations of Results

There is great interest in the use of anticoagulant therapy for coronary thrombosis. It is given for three reasons: (1) to forestall extension of thrombosis in the already thrombosed vessel and to prevent thrombosis in other vessels. It is generally agreed that dicumarol does not promote resolution of the clot which has already formed in a vessel; (2) to prevent the formation of mural thrombi (a source of emboli) on the endocardial surface of the area of infarction; and (3) to prevent thrombus formation in peripheral veins during the prolonged bed rest required for patients suffering from coronary thrombosis.

Solandt and Best suggested the use of heparin in coronary thrombosis in 1938. Wright in 1946 applied dicumarol for this purpose. Since then several papers have appeared, for the most part supporting the use of anticoagulants in this disease.

Gilbert, Fenn, and Nalefski have found that dicumarol has a vasodilator effect on the coronary circulation in anesthetized dogs which approaches that of the xanthines but is more prolonged Whether this effect plays any role in the amounts which are used therapeutically in the management of patients with coronary thrombosis has not been demonstrated.

RESULTS OBSERVED BY COMMITTEE ON EVALUATION Because the incidence of embolic phenomena in coronary thrombosis is not accurately known and because of the difficulty in determining with assurance the effect of the anticoagulants on the basis of isolated series of patients, The American Heart Association established a Committee for the Evaluation of Anticoagulant Therapy in the Treatment of Coronary Thrombosis with Myocardial Infarction. This Committee has collected enough material from different clinics to provide adequate numbers for statistical analysis.

Wright has recently summarized the results in 800 of these cases. Patients admitted to hospital on alternate days were treated with anticoagulants The deaths in the control group not treated with anticoagulants amounted to 22 per cent and in the treated group to 15 per cent; thromboembolic complications in the control group amounted to 24 per cent and in the treated group to 12 per cent. When correction was made for delays in diagnosis and for contraindications to treatment it was found the deaths amounted to 23 per cent in patients not treated with anticoagulants and to 13 per cent in the treated group, and the incidence of thromboembolic complications were 19 per cent and 9 per cent respectively. From this experience Wright advocated that all patients with myocardial infarction should be given adequate anticoagulant therapy.

In the analysis of the statistics comparing the mortality in the control with the treated group cognizance was not taken in each group of the numbers of patients of each age, of the sex distribution, of the presence of hypertension, of whether it was a first attack, as well as of other factors For instance it is known that the mortality rate in coronary thrombosis is greater in women than in men, and also greater in patients with hypertension than in those with normal blood

thrombin time. Since the development of the disease cannot be predicted in untreated patients it will be difficult to gauge the effectiveness of any treatment directed at specific prevention of recurrences of myocardial infarction. It is obviously impossible to prescribe a dicumarol regimen for all patients who have angina or for all patients one thinks might be threatened with coronary thrombosis

Prevention of Accidents in Use of Dicumarol

When a certain number of apparently unavoidable accidents occur from the use of dicumarol in well-regulated hospitals where special studies are being made and special care is exercised, it is a cause for much deliberation before recommending that this drug be given to all patients with myocardial infarction resulting from coronary thrombosis When hospitals cooperating in a study fail to measure up to certain precautions in estimation of the prothrombin time, it can hardly be expected that hundreds of laboratories with diverse standards will be able to provide the necessary safeguards which are required for the use of the drug. Care should be exercised that its use does not deteriorate into giving amounts of the drug which are *thought* to be within safe limits, even though the effect of such amounts on prolongation of prothrombin time may be inadequate to provide protection, thereby creating an unwarranted feeling of security about the proper treatment of the patient.

Rheumatic Mitral Stenosis and Auricular Fibrillation with Repeated Embolic Phenomena

In patients with chronic rheumatic heart disease, especially with auricular fibrillation, embolization from mural thrombi in the atrial appendages constitutes one of the most severe complications. Until recently no means were available for care of the acute episode and prevention of recurrences.

Embolic Phenomena

In such patients right atrial thrombi may give rise to pulmonary infarctions (hemoptysis, electrocardiographic changes) and left atrial thrombi to emboli in any part of the arterial tree. brain (paralysis), kidneys (lumbar pain, hematuria), mesenteric vessels (blood in stools, abdominal pain), and limbs (pain, loss of function, color changes). Moreover as a consequence of venous congestion in the lower extremities associated with heart failure, thrombi may form and may provide another source of emboli.

Regimen

Anticoagulant therapy should be started promptly when embolic phenomena [illegible]

[illegible] patient has sustained and if the patient has been carrying on satisfactorily, or has had previous embolic phenomena many years before with a long free interval, dicumarol may be discontinued after recovery from the current episode. If, on the other hand,

failure or auricular fibrillation occurs, even in the absence of thromboembolic phenomena.

4. In very severe myocardial infarction where there is evidence of extensive damage, especially if there is septal involvement with marked systemic symptoms such as shock in which there is a possibility that mural thrombi may form, anticoagulants should be used upon establishment of the diagnosis.

5. Anticoagulants are not used in patients who have had infarcts at intervals of several years unless there are evidences of thrombotic complications.

6. Anticoagulant therapy should be instituted in all patients who show evidence of thromboembolism or peripheral thrombophlebitis, provided there are no contraindications.

7 Anticoagulant therapy should be started in patients who have a series of infarctions at short intervals. It should not be used in the first infarction, but should be instituted upon evidence of further occlusions or extension of the infarction The general plan for the treatment and management of patients with coronary thrombosis is given in Chapter 13.

8 Since it is generally agreed that anticoagulants are effective in the treatment of thrombophlebitis and thromboembolic phenomena such as pulmonary infarction, it seems much more appropriate to treat patients with myocardial infarction due to coronary thrombosis in the usual manner without anticoagulants, and then to use the anticoagulants when occasion arises because of thromboembolic complications.

Method of Anticoagulant Therapy in Coronary Thrombosis

If anticoagulants are used an early effect is essential. To this end heparin and dicumarol should be administered at the same time, as described earlier in this chapter (p. 111). It seems best to give the heparin by the intermittent route intravenously, subcutaneously, or intramuscularly, rather than by continuous drip, in order not to increase the blood volume and thus put an additional burden on the heart and perhaps induce pulmonary edema. The intermittent subcutaneous route now appears to have taken precedence over the other methods.

Duration of Anticoagulant Therapy

Wright recommends that anticoagulant therapy be given routinely for a period of 30 days, and for at least 30 days after the last thromboembolic episode. I follow essentially the same regimen. In most instances I discontinue the drug several days before discharge from the hospital Other investigators give the drug for 21 days only, because studies have shown that the coagulation time is no longer accelerated 21 days after myocardial infarction.

Dicumarol as a Preventive

Recently dicumarol has been used in an attempt to forestall coronary thrombosis For this purpose it is being given to ambulatory patients on a ration or maintenance basis which has already been described (p. 109). On the basis of available evidence, however, it does not seem wise to put patients on ration doses of this drug because its use requires close supervision by the physician and frequent estimations of pro-

which this method can attain. Alcohol should not be used if dicumarol is being given;

10. Application of cold, by packing the limb in ice. This may have usefulness in certain cases, but I have had no experience with it;

11. Anticoagulants in accordance with the accepted program;

12. Creation of an arteriovenous fistula above the occlusion. This is a new approach in the treatment of certain of the arterial occlusions of the foot and lower leg. Improvement in the peripheral circulation has followed in certain instances. The rationale of this procedure is the increase in blood supply in a normal extremity which ensues after the accidental formation of an arteriovenous fistula Unfortunately, though, if too large a fistula is made the strain on the heart may be more than can be tolerated, and if the opening is too small it has been found that it does not remain patent. The indications for this form of therapy will have to be determined by careful study.

Cerebral and other localizations of emboli are treated in the appropriate manner.

Peripheral Venous Occlusions and Thrombophlebitis

In peripheral venous occlusions or thrombophlebitis some of the following measures may be indicated·

1 *Elevation of the part* provides tissue drainage so that edema fluid does not accumulate and increase circulatory stasis

2 If there is evidence of inflammation moderate elevation of temperature by dry heat or by *moist warm compresses* may be useful

3 *Penicillin* in adequate amounts may be given to patients with thrombophlebitis when there is inflammation It is also administered if pulmonary infarction occurs in order to prevent secondary pulmonary infection

4 Surgical ligation of the veins may be indicated Before the introduction of anticoagulants, ligation of the deep veins for thrombophlebitis had become a fairly common procedure in certain clinics In fact, the deep veins were often ligated as a preventive measure before operations—a practice which I do not recommend If there is evidence of a large and growing thrombus, it is best to ligate the deep veins and perform an embolectomy before it becomes dislodged This may be required even when anticoagulant therapy is used, since it is recalled that *there is no evidence that the anticoagulants dissolve or dissipate clots*

Anticoagulants and Quinidine in Auricular Fibrillation

The most frequent irregular rhythm of those requiring conversion to normal rhythm is auricular fibrillation Before attempting to alter the rhythm the possibility that the patient may be better off and his ventricular rate be more easily controlled with the auricular fibrillation should be considered However, it will be seen in Chapter 5 that the incidence of atrial thrombi is increased after prolonged auricular fibrillation or heart failure There is the potential danger, therefore, that the regular coordinated contraction of the atrial appendages may dislodge thrombotic material and precipitate embolic phenomena on reversion of auricular fibrillation to normal rhythm. It has been suggested that dicumarol or heparin may be given before reversion is attempted, in order to increase the clotting time while quinidine or other

the patient has had repeated episodes at fairly short intervals during the last year, ration amounts of dicumarol may be continued after recovery from the current episode. As the patient becomes ambulatory and is discharged from the hospital the ration doses are maintained. If this procedure is decided upon, the drug is given as described for the ambulatory regimen, all of the appropriate precautions being observed. Wright and his associates have been accumulating data on the efficacy of ambulatory treatment with dicumarol in such patients. It is recalled that many of these patients suffer embolic phenomena very infrequently, years often elapsing between episodes. It does not appear justified to give a drug which requires such close supervision over a period of years to a patient exhibiting this pattern, especially since its usefulness cannot be gauged. In patients with frequent embolic episodes, however, anticoagulants should be given a trial.

PERIPHERAL ARTERIAL OCCLUSIONS

On appropriate occasions certain of the following measures may find application in patients exhibiting peripheral arterial occlusions:

1. The suction pressure boot, for alternating pressure in the extremity;

2 Surgical embolectomy,

3. Paravertebral lumbar sympathetic block, to increase the vasodilatation in the accessory circulation and encourage the development of collateral vessels;

4. Tetraethylammonium (TEA) or dibenamine, which may provide temporary or transient increases in the accessory or collateral circulation. When temporary increase in peripheral blood flow of the whole body occurs, the affected part may share in it through the vessels which remain patent; these drugs act by blocking the autonomic ganglia;

5. Papaverine in adequate amounts may induce vasodilatation; it should be used with great care, because its intravenous injection has resulted in death, probably due to ventricular fibrillation;

6. Priscoline, a new sympatholytic drug which has been used as a vasodilator It is said to increase peripheral blood flow by counteracting the constrictive effect of epinephrine-like substances at the vascular myoneural junctions Priscoline is available for oral or parenteral administration, 25 mg being given at three- to four-hour intervals. If satisfactory response is not obtained and there are no distressing side reactions the dose can be increased to 50 mg The effects of the drug are shown in flushing of the face and upper trunk, warming of the extremities, increase in heart rate, slight rise or fall in blood pressure, pilomotor activity, increased peristalsis, postural hypotension, and decrease in response to pressor stimuli It should not be used in patients with known coronary artery insufficiency;

7. Maintenance of the part at body temperature. Its temperature should not, however, be increased by using a cradle light; rise in temperature of the part increases its tissue metabolism and demands an increased circulation which the available arterial channels may not be able to provide;

8. Keeping the part on a level with the heart, neither elevated so that it blanches, nor lowered so that stasis occurs;

9 Liberal amounts of alcohol, which may provide the maximal vasodilatation

as possible, will avoid peripheral stasis. (7) The patient should not sit propped up in bed so that the deep veins are encroached upon. (8) In the use of early mobilization patients should be encouraged to walk around frequently. They should not sit quietly in a chair because this results in venous stasis and may be more harmful than lying in bed.

Axillary Vein Thrombosis

Axillary vein thrombosis results from trauma to the vein, usually by sudden stretching. It may follow exercise requiring hyperextension of the arms, as during dumb-bell exercises, working on parallel bars, or sudden lifting It occurs more commonly on the right side and is more frequent in males. Surgeons sometimes speak of it as "effort syndrome" or "effort thrombosis" because it is frequently a consequence of severe or unaccustomed exertion This use of the first term should be discouraged in order to avoid confusion with the long-established use of "effort syndrome" as a synonym for neurocirculatory asthenia. Occasionally axillary vein thrombosis may be associated with the scalenus anticus syndrome It may result from spasm.

Swelling of the arm is the most common symptom, with pain next in frequency. In many instances the area becomes cyanotic and the superficial veins are prominent and do not empty when the arm is raised There is swelling of the hand and arm, a palpable venous cord can frequently be felt, and the extremity is cooler than the unaffected side The venous pressure is elevated on the affected side.

If visualization with a radio opaque substance is carried out, the material should be diluted in order not to induce further thrombosis This should differentiate stricture due to scalenus anticus syndrome from axillary vein thrombosis.

Removal of a section of the affected vein in certain instances has not demonstrated a clot, but only narrowing and constriction of the vessel.

The most comfortable position is for the arm to be elevated and kept at rest Local hot, moist applications are used. The clot does not propagate and does not loosen, but *anticoagulants* may be used in order to keep the small collateral vessels open Sympathetic block may be carried out but it is doubtful that it will be of benefit. Recovery is slow and is accomplished by re-establishment of collateral circulation in the shoulder.

Dicumarol in Congestive Heart Failure

It is well known that prolonged congestive heart failure predisposes to the development of venous thrombosis and embolic phenomena. Indeed, one wonders how the majority of these patients can go on for years without experiencing these manifestations Peripheral venous thrombosis may occur because of sluggish circulation and the compression of veins by edema, mural thrombi are especially prone to form in the presence of auricular fibrillation, especially in patients with large auricles who suffer from mitral stenosis

Recently Wishart and Chapman have reported the use of dicumarol in patients with congestive heart failure The principal etiologic factor in most of the patients they observed was arteriosclerosis, in others it was rheumatic fever, and in a few hypertension together with arteriosclerosis They aimed to keep the prothrombin

drugs are being used to obtain reversion to normal rhythm. However, it has not yet been demonstrated that this precaution will eliminate the risk of embolization One must also bear in mind that patients receiving quinine derivatives may have elevated prothrombin times and may show a marked response to the usual doses of dicumarol.

Subacute Bacterial Endocarditis

Anticoagulants are not generally advised in the treatment of subacute bacterial endocarditis In the first place, results of treatment are satisfactory without anticoagulants; there is no evidence that recovery is facilitated by their use Second, there is the not unreal danger of hemorrhage from their administration in this disease This possibility is sufficiently grave to outweigh the reports that penicillin promotes thrombosis.

Prevention and Treatment of Thromboembolic Diseases

The opinion is general that anticoagulants should be used promptly in the treatment of thrombophlebitis, pulmonary infarction even though the source of the emboli may not be apparent, and thrombophlebitis with pulmonary infarction. Anticoagulants are used not with the notion of altering the clot which has already formed but in order to prevent its extension, the formation of additional thrombi, and embolic phenomena. If a clot remains in a vessel for several hours it is likely that adherence to the wall is firm enough to prevent it from becoming a source of emboli, in short, emboli arise from fresh unattached thrombi. Heparin and dicumarol should be used together in the manner which has been described It is the opinion of most observers that extension of the thrombophlebitis is halted and that fatal embolization rarely occurs when adequate amounts of these drugs have been used.

There is a growing experience with the use of these drugs postoperatively upon the appearance of thrombophlebitis and pulmonary infarction. Some investigators recommend their routine use postoperatively to prevent such accidents in patients who give a history of previous thrombosis or embolism In such patients dicumarol is continued until the patients have been ambulatory for several days or until they are ready to leave the hospital. It is recalled that early ambulation after surgical operations has been thought to decrease the frequency of thrombophlebitis and pulmonary infarction. There are, however, some observations which do not bear this out. When anticoagulants are used in the postoperative period the danger of hemorrhage is to be kept in mind.

Attention to the following measures after operations will tend to prevent peripheral venous thrombosis and thrombophlebitis.

(1) Tight abdominal and chest binders should be avoided. (2) Tight tourniquets should not be applied to the legs (3) Rebreathing 100 per cent oxygen increases expansion of the lungs and minimizes pulmonary stasis in the quiescent portions of the lungs. (4) Breathing deeply six to ten times at hourly intervals throughout the waking hours may also be effective in maintaining expansion of the lungs. (5) The patient should be turned frequently to avoid stasis in the pulmonary peripheral circulation. (6) Elevation of the legs, together with leg and body exercises as soon

We were recently confronted with the problem of a patient 27 years of age with mitral stenosis and insufficiency and aortic insufficiency who was four months pregnant She had auricular fibrillation, a relatively late complication of mitral stenosis, and had suffered an arterial embolism to the right leg, presumably from a mural thrombus in the left auricle The heart was large and had increased in size in the last two years Pregnancy is contraindicated in patients with mitral stenosis, mitral insufficiency, and aortic insufficiency, especially in the presence of auricular fibrillation and in those with embolic manifestations Anticoagulant therapy was instituted to aid in the current emergency. Interruption of the pregnancy was not to be considered at the time of the embolus to the right leg Pregnancy had progressed too far for vaginal interruption to be employed It appeared better to have the patient continue with the pregnancy to term, under careful supervision and in bed Dicumarol was continued until three days before delivery, which was normal and spontaneous, the second stage being shortened by the use of low forceps. Dicumarol was started again 24 hours later and was given to the patient on an ambulatory schedule for some weeks afterward.

SUMMARY

The use of anticoagulant drugs has opened up a new field in the treatment of thrombotic complications of many diseases There are certain drawbacks to the use of the two anticoagulant drugs in most common use now available, heparin and dicumarol The difficulties in the use of heparin lie in the routes by which it must be given and in its cost When given by intermittent injection subcutaneously, intramuscularly, or intravenously, fluctuations in the clotting time of the blood occur. The difficulties of the continuous intravenous technic are obvious On the other hand, although dicumarol is given orally, it has the drawback of requiring 48 to 72 hours for a full effect, its effect persists for many days after the drug has been discontinued, and the laboratory technic of estimating the effect on prothrombin time are subject to errors No doubt continued research will result in finding drugs which do not have the same disadvantages It has already been found that tromexan induces its effects more quickly and is dissipated more rapidly than dicumarol, and in certain instances may be substituted for it with advantage

The opinion is general that anticoagulants should be used in the presence of *thrombophlebitis and thromboembolism.*

Anticoagulants may be indicated in certain instances of coronary thrombosis with myocardial infarction It does not appear wise, however, at the present time to give these drugs to every patient with myocardial infarction What the final recommendation may be awaits further experiences with these and other anticoagulants

Evidence is lacking to support the use of anticoagulants in patients with angina or after recovery from coronary thrombosis in order to prevent subsequent attacks

Anticoagulant drugs are recommended for patients with mitral stenosis with or without auricular fibrillation who suffer repeated pulmonary infarctions It may appear in order to give dicumarol after the patients are ambulatory to prevent subsequent attacks if the frequency of such attacks can justify its use.

concentration below 30 per cent and above 10 per cent, as suggested by Allen and his associates The average initial prothrombin concentration before dicumarol was started was 62 per cent of normal. In one patient it was only 17 per cent; this was interpreted as further evidence that liver function may be significantly impaired in congestive heart failure The initial dose of dicumarol was 200 mg. Heparin was given intramuscularly for the first 24 to 48 hours to a few patients. Dicumarol was continued on the usual schedule until the patient was ambulatory or until death supervened Smaller doses of dicumarol were required in patients who had heart failure than are required in compensated patients. Hemorrhagic complications were not encountered although it was necessary in some of the cases to discontinue dicumarol because of excessive depression of prothrombin concentration. Vitamin K in 30-mg amounts intravenously three or four times daily was occasionally used to counteract the dicumarol effect.

Kinsey and White have reported the natural history of patients with heart failure whom Wishart and Chapman considered comparable to their patients. In that series embolic phenomena in the form of pulmonary infarcts occurred in 22 per cent of the patients, whereas in the treated series which Wishart and Chapman reported the incidence was only 6.5 per cent Kinsey and White concluded that dicumarol probably gives protection from thrombosis and embolism when the patient is in congestive heart failure The final place of this regimen in the treatment of patients with congestive heart failure has not yet been established.

Anticoagulants During Pregnancy

It is fortunate that most of the complications which require the use of anticoagulants do not occur frequently in pregnant women Coronary thrombosis is of rare occurrence in women in the childbearing age This accident is discussed in Chapter 28 (p. 490). It will be recalled that dicumarol is the cause of hemorrhagic disease of pregnant and nonpregnant cows Recent studies of Kraus, Perlow, and Singer in animals indicate that the prothrombin level of the fetus is affected to a much greater extent than that of the mother, but they recognize that their animal experiments may not find direct application to human beings These authors nevertheless think that the data suggest that dicumarol therapy should not be carried out in pregnant women as it may interfere with the normal fetal development or cause fetal death. The opinion is general, nevertheless, that with careful supervision the drug may be used up to the sixth week before the expected date of delivery (recently this point of view has been liberalized still further) The drug should not be given during pregnancy without mature consideration of the dangers involved

There has been more experience with the use of anticoagulants in thrombophlebitis occurring during the course of pregnancy than with myocardial infarction Wright has carried 50 mothers through various stages of pregnancy with thrombophlebitis without losing a baby and without fetal deformities. Four months was the longest continuous maintenance on dicumarol In order to be on the safe side it is better to keep the prothrombin time around 25 seconds, rather than at the optimal level of 30 to 35 seconds. It is probably best to discontinue dicumarol two days before delivery and start again afterward, in order to avoid hemorrhage, although this precaution has been neglected by some observers without ill effects

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The use of anticoagulants prior to the administration of quinidine in patients with abnormal rhythms and its administration in congestive heart failure is still experimental.

It is generally agreed that anticoagulants should not be used in subacute bacterial endocarditis.

Anticoagulants have opened a new field in therapy, but the routine use of these drugs should be discouraged. They should only be used after deliberate evaluation of the indications and contraindications in the particular patient under consideration Accidents have occurred from the use of dicumarol even when the drug is give under unusually close guidance of a special study, with special emphasis on dosage and prothrombin time. Death has resulted from hemorrhage into serous cavities such as the pericardium, and from intravascular clotting due to the use of vitamin K to counteract overdicumarolization Even though such accidents may be infrequent they cannot be ignored in making a general recommendation that the drug be used routinely.

One cannot overstress the warning that the drugs should be used only under close clinical observation and only when proper and accurate laboratory supervision is available.

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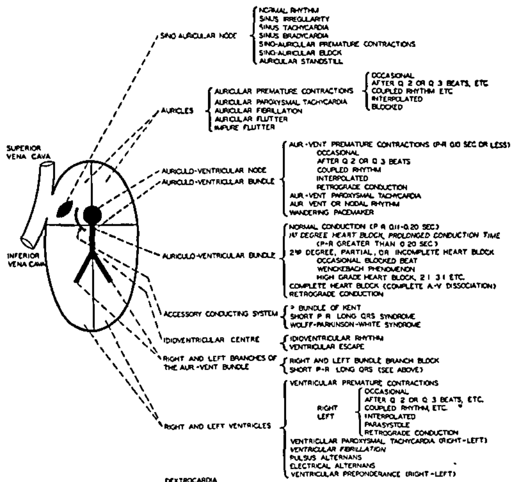


Fig 20

Rhythms of the Heart Most Frequently Encountered and Sites of Their Origin. (Stewart, H J. "Functional Disorders of the Heart Cardiac Arrhythmias," in *Cecil's Textbook of Medicine* (Ed 7), Philadelphia, Saunders, 1947, p 1247)

Recently, Glomset and his associates have questioned the validity of our present notions about the morphology of the conducting system of the heart. On the other hand Kistin has presented data reaffirming the current point of view.

In Figure 20 is reproduced a diagram listing the common cardiac rhythms which are frequently encountered and their sites of origin in the heart Most of these rhythms will be described and many of them illustrated in the following pages.

CHAPTER 5

Irregularities of the Heart

INTRODUCTION

Whenever possible an accurate diagnosis of a cardiac arrhythmia should be made before attempting specific treatment for its correction How much can be done toward making an exact diagnosis will vary with the circumstances. While the electrocardiogram offers the most accurate diagnostic aid it is not always possible to obtain records during an attack If the physician makes a careful clinical examination first and then checks the findings with electrocardiograms whenever possible he will acquire a skill which will frequently allow him to make the correct diagnosis when electrocardiograms are not available Paroxysmal rhythms are often of brief duration and may not last long enough to be observed by the physician or for an electrocardiogram to be taken For patients who have been having attacks over a long time without a diagnosis having been made, we make arrangements to have them come to the emergency department of the hospital at any time, day or night, for an electrocardiogram to be taken when the abnormal rhythm comes on.

In order to understand and treat the irregularities of the heart, the physician *should keep in mind the physiologic properties of heart muscle* The heart beat is the expression of a physiologic mechanism and pathologic variations of the heart beat have no histologic counterparts that our present technics are able to detect, except occasionally in the case of heart blocks. Many irregularities do not require treatment, on the other hand certain of them require urgent and precise treatment. The pathologic physiology of the irregularities and the circumstances under which they occur must always be kept in mind.

The normal stimulus initiating the heart beat arises in the sino-auricular node, which *lies in the right auricle in the region of the opening of the superior vena cava.* This stimulus spreads in a radial fashion over the auricles and initiates their contraction, and arriving at the auriculoventricular node, passes rapidly down the auriculoventricular bundle and over its right and left branches, to be distributed by the

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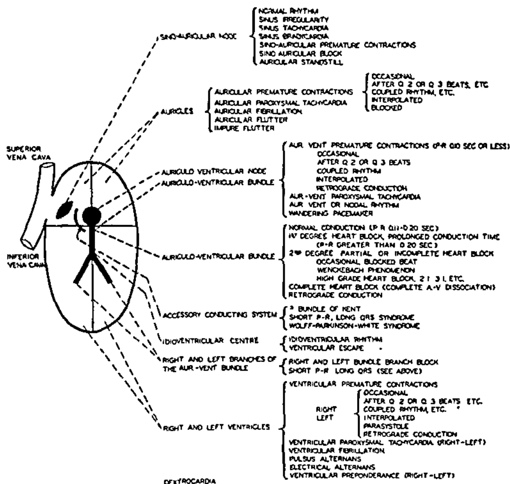


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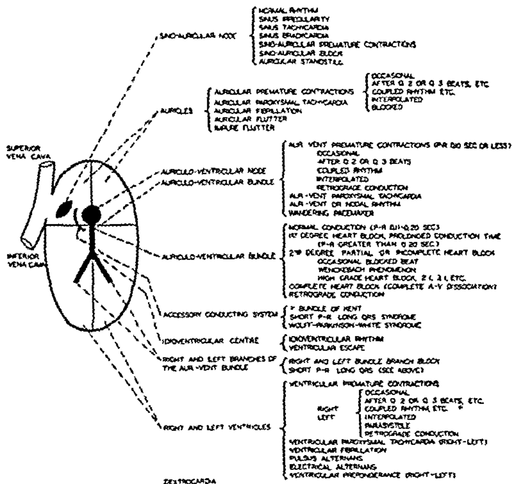


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NORMAL SINUS RHYTHM

The heart beat controlled by the sinus node is designated by the following terms: *normal rhythm, normal sinus rhythm, normal (sinus) mechanism,* and *regular (sinus) rhythm.* Modifications of this basic rhythm are expected under certain circumstances; there may be an association of certain rhythms with certain diseases. Under these conditions treatment might not be required for the rhythm per se but for the underlying cause or disease.

Sinus Irregularity

Sinus irregularity is said to be present when the discharge of impulses from the sinus node occurs irregularly, so that the heart rhythm is irregular. Usually the discharge waxes and wanes with inspiration and expiration, so that a respiratory pattern can be detected. It is a physiologic phenomenon in children and young adults. It may disappear in rheumatic carditis or be exaggerated by digitalis. It, of course, requires no treatment.

Sinus Tachycardia

Sinus tachycardia, which may be induced by events such as exercise, eating, excitement, and fear, is said to be present when the discharge of impulses from the *sinus node is greater than 100 per minute. Under these conditions it is a normal* physiologic phenomenon. However, when the rate exceeds normal expectation inquiry should be made into the cause and appropriate therapy instituted. Sinus tachycardia occurs as a sign in many diseases, the more common of which are fever, anxiety, neurocirculatory asthenia, anemia, tuberculosis, Graves' disease, infections (except typhoid fever), rheumatic fever, myocardial infarction, congestive heart failure, hemorrhage, and shock. In some instances therapy must be directed at the relief of distressing symptoms. Sedatives, particularly phenobarbital, may be beneficial.

The use of *neostigmine* has been recommended for sinus tachycardia when it gives rise to disturbing symptoms. It is given intramuscularly in 1.0-mg amounts (2.0 cc of a 1:2000 solution). Sinus tachycardia with the sensation of pounding may be an expression of deep-seated anxiety, fear, or alarm, under these circumstances it may require expert psychiatric help to arrive at an understanding of the underlying *cause and the gaining of insight by the patient.*

When sinus tachycardia disturbs the patient after lumbodorsal sympathectomy in hypertension, slowing of the heart rate can be obtained by bilateral *upper thoracic sympathetic ganglionectomy* from the inferior cervical ganglion through the fourth thoracic ganglion. The heart rate slows to around 50 per minute and under exercise increases to around 60 per minute. After some months the resting rate may rise to 60 per minute. These patients treated with complete sympathectomy get on very well, though perhaps they do not bear extreme hot or cold weather as well as normal subjects. The interruption of accelerator nerve fibers in the treatment of the tachycardia is discussed more fully at the end of this chapter (see pp. 186–187).

Sinus Bradycardia

Sinus bradycardia is said to be present when the sinus discharge falls to 60 per minute or lower. Its occurrence during sleep, in athletes, and in young adults is physiologic. When it occurs in such conditions as malnutrition, jaundice, brain tumor, meningitis, and cerebral hemorrhage, the etiologic disease is appropriately treated. When it is due to digitalis the drug may be omitted for a few days. If this is the only manifestation of sensitivity of a carotid sinus it usually does not require therapy (Chapter 25). It is rarely necessary to use atropine. At times the *sinus discharge may be so slow that there is ventricular escape (see p. 171).*

Sino-auricular Block

In sino-auricular block—sinus pause or cardiac arrest—the sinus node fails to discharge a stimulus, and the heart fails to beat This may occur for one expected beat, so that the pause is approximately equal to two cardiac cycles, or the block may be of greater duration and may result in symptoms of dizziness or even syncope. Occasional sino-auricular block requires no therapy. When the attacks are due to *digitalis*, the drug is discontinued or the dose reduced, if the attacks occur only rarely, and digitalis is required to control heart failure, this drug should be continued When it is occasioned by *quinidine* or by *potassium salts*, they are discontinued

If sino-auricular block results from *hypersensitivity* of one or both *carotid sinuses* (Fig 57 A and B) and is associated with symptoms of dizziness, syncope, and perhaps convulsions owing to cerebral anemia, the patient is warned to avoid the maneuvers which precipitate an attack sudden turning of the head, a tight or high collar, bending the neck forward, or sitting in a low club chair when reading These symptoms result from decrease in or cessation of cardiac output with cardiac arrest; as an expression of this the blood pressure falls and may be unobtainable. If attacks occur frequently and under circumstances prone to accidents *atropine* 0.0006 Gm three times a day (Fig 57 C and D), Tr belladonna 0.06 to 1.0 cc three times a day, ephedrine 20 to 30 mg. three times a day, or phenobarbital 0.015 Gm. four times a day may be effective in preventing them If these measures are ineffective, two surgical procedures are available· (1) one or both carotid sinuses may be denervated (Chapter 25), (2) the ninth nerve may be sectioned intracranially on the more sensitive side (Fig. 59 A and B), a procedure which Ray thinks is more effective than denervation of the carotid sinus One carotid sinus is usually more sensitive than the other.

Auricular Standstill

This rhythm is of uncommon occurrence Most of the instances we have encountered have been due to the toxic effect of potassium ions on heart muscle *Potassium salts* have a toxic effect on the sinus node As a consequence all activity ceases in this node and death results when the idioventricular center or a focus in the ventricles fails to take over or to continue pacemaking; the ventricular rhythm is usually slow and irregular Aberration of conduction through the ventricular muscle is a distinctive feature. In one instance it resulted from the

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intravenously This results in increase in excretion of potassium and in recovery of the heart muscle from damage caused by this ion. One of the cationic exchange resins (without potassium) may be a useful adjunct in removing potassium from the blood.

Auricular standstill may also result from *quinidine* (Fig. 22 D) or *digitalis*. When one of these is implicated its use should be discontinued.

AURICULAR RHYTHMS

Auricular Premature Contractions

"Premature contraction" is the best term to apply to an irregularity of the heart rhythm due to abnormal stimuli arising in various parts of the heart, usually occurring before the expected beat and therefore premature The term *extrasystole* implies an extra beat of the heart, and is applicable only when a beat occurs between two normal beats without disturbing their sequence. If the premature contraction occurs early there is usually a pause until the next usual beat, or if the premature contraction occurs late, the beat takes the place of the expected one in counting the number of heart beats.

The terms "ectopic" and "aberrant" are not inclusive since they would not suffice in the case of a premature contraction arising in the sino-auricular node, which is the normal site of impulse formation. Premature contractions arising from the sino-auricular node are, however, uncommon. "Intermittent pulse" is a vague term and does not convey an accurate meaning of the cardiac rhythm "Dropped beat" may be used with accuracy only in referring to heart block, when a sinus impulse is blocked from reaching the ventricles, and the ventricles fail to beat.

Auricular premature contractions result from abnormal stimuli arising in one of the auricles, which initiate premature contractions in them and, passing down the auriculoventricular conduction system, stimulate contractions of the ventricles. The premature complex is recognized in the electrocardiogram by a P wave of different contour from the normal P waves in this lead, with a P-R time of 0.11 seconds or more, and a QRS complex of the supraventricular type, although it may differ from the usual ones in this lead The P waves may be negative. Auricular premature contractions may occur singly, in a repeated pattern to give coupling or trigeminy, and several in a sequence In certain instances the auricular impulse may be blocked

Auricular premature contractions may be asymptomatic and without significance and therefore require no treatment They may occur in acute infectious diseases such as pneumonia, in active rheumatic carditis, and in organic affections of the heart such as mitral stenosis and coronary artery disease They may disappear with recovery from the acute process or remain with the chronic cardiac disease They may occur during periods of stress and disappear with their passing. When these contractions are due to the increased use of coffee, alcohol, or tobacco, or the combination of any of these, the agents implicated should be restricted or their use eliminated Attention should not be directed to premature contractions if the patient is unaware of them or has no symptoms.

use of potassium chloride as a diuretic in a patient with heart failure in whom the renal function was decreased (Fig. 21). Cardiac standstill led to the patient's death. In a second instance it occurred in a patient to whom potassium bicarbonate was given as a substitute for sodium bicarbonate when sulfadiazine was being administered (Fig. 64). The potassium salt was discontinued and the patient recovered A third instance *occurred in a young boy with the nephrotic syndrome* in the presence of decreased renal function. There was temporary remission but this patient died.

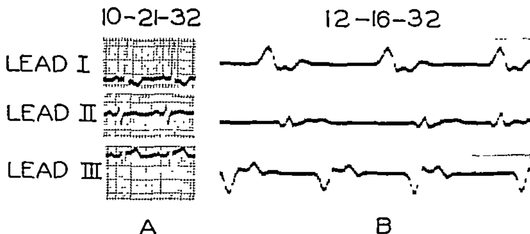


FIG 21.

Arteriosclerotic Heart Disease with Heart Failure in a Woman 54 Years of Age

...ence of digitalis.
fter receiving
per minute
Evidence of
st derivation
ed, the QRS

J Changes
use of potassium salts

Potassium salts should be used *with great care, especially in* patients in whom the renal function is reduced and the excretion of potassium is retarded Cardiac standstill may occur without the use of potassium salts when the renal function is greatly decreased *and the excretion of potassium is impeded so* that the serum potassium rises to levels which are toxic for the heart muscle. Cardiac standstill with bizarre ventricular rhythm has been found to occur when the serum potassium is around 10 mEq *When potassium is implicated, the use of the salt which is* responsible should be discontinued. *Calcium chloride* 0.5 Gm intravenously or barium *chloride* 30 to 40 mg. orally may increase cardiac irritability. The most effective treatment, however, *is the prompt administration of glucose and saline*

Toxic Effects of Quinidine in Treatment of Ventricular Premature Contractions in a Man 53 Years of Age With poisoning of the sinus and auriculoventricular nodes there was auricular standstill, and of the intraventricular conducting system there was bundle branch block Discontinuance of quinidine resulted in restoration of normal rhythm and of normal intraventricular conduction

A, taken on August 30, 1945, showed normal sinus rhythm The QRS time was 0 10 second Left axis deviation was present

B, taken September 22, 1945, showed occasional ventricular premature contractions. The QRS time was 0 10 second Following this record quinidine was given orally because of the ventricular premature contractions

C was taken September 23, 1945 at 3 15 p m., 24 hours later, after the patient had received a total of 2 2 Gm of quinidine The amplitude of the QRS complexes had decreased The QRS time was now 0 11 to 0 12 second The use of quinidine however was continued even though bundle branch block had appeared probably as a toxic manifestation of quinidine

D was taken on September 25, 1945, the patient having had 0 4 Gm quinidine q 4 h since September 23, 1945 There was absence of auricular activity and apparently auricular standstill was present as a manifestation of quinidine intoxication The QRS time had increased at this time to 0 18 second indicating an increase in difficulty in the spread of the excitation wave In the first three leads of this electrocardiogram the time marker was running double speed, but this was taken into account in calculating the QRS time Quinidine was discontinued on this date after this electrocardiogram had been recorded

E was taken on September 26, 1945, 24 hours later There was still no evidence of sinus activity, auricular standstill being present The QRS time was 0.16 second, the intraventricular conduction defect remaining

F, recorded on October 3, 1945, showed that normal sinus rhythm was present, the activity of the sinus node having been restored and the QRS time had returned to 0 10 second The configuration of the electrocardiogram was somewhat similar to that prevailing before quinidine was started

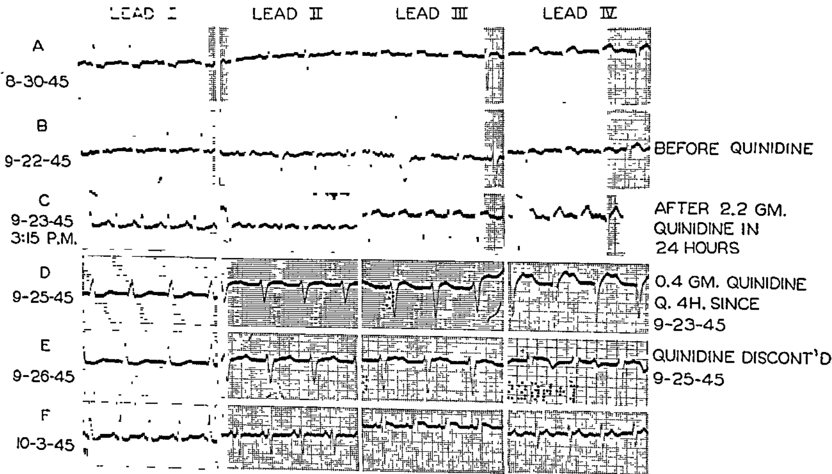

LEAD I
LEAD II
LEAD III
LEAD IV
A
8-30-45
B
9-22-45
BEFORE QUINIDINE
C
9-23-45
3:15 P.M.
AFTER 2.2 GM.
QUINIDINE IN
24 HOURS
D
9-25-45
0.4 GM. QUINIDINE
Q. 4H. SINCE
9-23-45
E
9-26-45
QUINIDINE DISCONT'D
9-25-45
F
10-3-45

Fig 22

Effects of Different Forms of Therapy in a Woman 29 Years of Age with Rheumatic Heart Disease who Had Attacks of Auricular Paroxysmal Tachycardia

A Leads I, II and III during auricular paroxysmal tachycardia The rate was 167 The P waves are indicated The standardization was such that 1 cm. deflection of the string equaled 1 millivolt B Leads I, II, and III, taken immediately after the above The speed of the film was increased so that the complexes were spread apart and the P waves were more easily identified The standardization was 1 cm equaling 1 millivolt C Lead I during auricular paroxysmal tachycardia Immediately after this record was taken mecholyl 0.25 mg was given subcutaneously

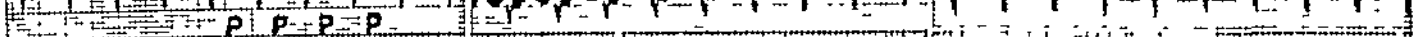
Records from C to D were continuous Following mecholyl there was reversion to normal sinus rhythm with 2:1 heart block except for one cycle. E is a continuation of the preceding record showing normal sinus rhythm with transient bundle branch block There were transient reversions to auricular paroxysmal tachycardia

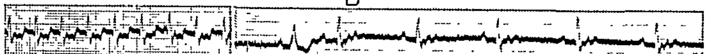
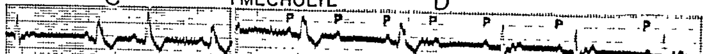
In *F* carotid sinus pressure was applied Following this, again in Lead I, there was reversion to normal sinus rhythm with 2:1 heart block and bundle branch block for the next four P waves followed by 2:1 auriculoventricular block with normal QRS conduction time *G* is a continuation of *F* after an interval *Normal sinus rhythm was present at the beginning of the record with occasional premature contractions followed* by blocked P waves after which there was a reversion to auricular paroxysmal tachycardia at the end of the record which persisted *H* shows Lead I of the same attack of auricular paroxysmal tachycardia

Electrocardiograms A to *H* inclusive were taken on February 26, 1936 and were portions of continuous records

It was apparent that neither mecholyl *alone nor re enforced with carotid sinus pressure caused persistent reversion to normal rhythm* and digitalization was decided upon

The patient was given 0.8 Gm of digitalis leaf at 8:00 P.M. on the evening of February 27, 1936 Normal rhythm had been restored at 11:00 P.M. that evening An additional 0.5 Gm was given at 8:00 A.M. on February 28, 1936, and 0.3 Gm at noon of February 28, 1936 The patient had received a total of 1.6 Gm when electrocardiogram I was taken, which shows Leads I, II, and III after reversion to normal sinus mechanism Further digitalis was not given and normal rhythm persisted




LEADS
I II III
P P P P
A
I II III
P P P
B
I
C
MECHOLYL
D
I
P P P P P P P
E
CAR. SIN. PRES. F
I
DIG. 1.6 GM. AFTER H
G
H
I II III
I

Fig 23.

Effects of Different Forms of Therapy in a Woman 29 Years of Age with Rheumatic Heart Disease who Had Attacks of Auricular Paroxysmal Tachycardia

A Leads I, II and III during auricular paroxysmal tachycardia The rate was 167. The P waves are indicated The standardization was such that 1 cm. deflection of the string equaled 1 millivolt *B* Leads I, II, and III, taken immediately after the above The speed of the film was increased so that the complexes were spread apart and the P waves were more easily identified The standardization was 1 cm equaling 1 millivolt *C*: Lead I during auricular paroxysmal tachycardia Immediately after this record was taken mecholyl 0 25 mg was given subcutaneously

Records from C to D were continuous Following mecholyl there was reversion to normal sinus rhythm with 2 1 heart block except for one cycle. E is a continuation of the preceding record showing normal sinus rhythm with transient bundle branch block There were transient reversions to auricular paroxysmal tachycardia

In *F* carotid sinus pressure was applied Following this, again in Lead I, there was reversion to normal sinus rhythm with 2 1 heart block and bundle branch block for the next four P waves followed by 2 1 auriculoventricular block with normal QRS conduction time *G* is a continuation of *F* after an interval Normal sinus rhythm was present at the beginning of the record with occasional premature contractions followed by blocked P waves after which there was a reversion to auricular paroxysmal tachycardia at the end of the record which persisted *H* shows Lead I of the same attack of auricular-*paroxysmal tachycardia*

Electrocardiograms *A* to *H* inclusive were taken on February 26, 1936 and were portions of continuous records

It was apparent that neither mecholyl alone nor re enforced with carotid sinus pressure caused persistent reversion to normal rhythm and digitalization was decided upon

The patient was given 0 8 Gm of digitalis leaf at 8 00 P M on the evening of February 27, 1936 Normal rhythm had been restored at 11 00 P M that evening An additional 0 5 Gm was given at 8 00 A M on February 28, 1936, and 0 3 Gm at noon of February 28, 1936 The patient had received a total of 1 6 Gm when electrocardiogram *I* was taken, which shows Leads I, II, and III after revision to normal sinus mechanism Further digitalis was not given and normal rhythm persisted

Treatment of Symptoms

When symptoms arise from auricular premature contractions, *triple bromide* (sodium, potassium, and ammonium) 1.0 Gm. three times a day may cause them to disappear. When symptoms have been relieved the dosage may be decreased and finally the drug may be discontinued. The patient is warned of drowsiness and pustular skin rash. *Phenobarbital* 0.015 Gm. three times a day may be beneficial. If the use of sedatives is ineffective, *digitalis* in full therapeutic amounts is the most useful drug *Quinidine* 0 2 Gm. three times a day is not so effective as it is in the relief of ventricular premature contractions. If *potassium chloride* or phosphate 2.0 Gm. three times a day is used for this purpose, auricular standstill as a toxic effect of potassium must be kept in mind *Papaverine* 0.06 to 0.3 Gm. three to four times a day at three- to four-hour intervals may abolish the premature contractions.

Auricular Paroxysmal Tachycardia

"Paroxysmal tachycardia" is the name applied to a variety of rhythms of the heart which are characterized by sudden onset and sudden offset. Usually the heart beats at a rapid rate. While the diagnosis of paroxysmal tachycardia can be made from the description which a patient gives of an attack it is not possible to decide upon place of origin in the heart without seeing the patient during an attack, and diagnosis can only be made with certainty by means of an electrocardiographic tracing. Usually the term paroxysmal tachycardia is reserved for the tachycardias which arise in the auricles, in the auriculoventricular conducting system, and in the ventricles. On the other hand auricular fibrillation and auricular flutter may be paroxysmal or transient and therefore must be included in the differential diagnosis. The onset of any of the paroxysmal rhythms may be associated with *syncope*

I have deliberately set the various types of paroxysmal tachycardias apart from each other and discussed the treatment of each under the abnormal rhythms arising in the different parts of the heart. This is to encourage differentiation and to emphasize the fact that these tachycardias have for the most part different origins and different methods of treatment, even though in some instances the same drugs may be used.

Paroxysmal tachycardia may be transient, lasting for a few beats only, or attacks may persist for as long as years. Campbell thinks that the term paroxysmal tachycardia should not be used as a designation for the rapid abnormal rhythms which are persistent. He suggests the term "protracted tachycardia."

Auricular paroxysmal tachycardia is a rapid, regular beating of the heart arising from a focus in the auricles, characterized by sudden onset and sudden offset In electrocardiograms, P waves of abnormal form are recorded with the P-R interval exceeding 0 10 *seconds (Fig 23 A and B). The QRS complexes usually have a* supraventricular form. The ventricles usually respond to all the stimuli but varying grades of heart block, including Wenckebach phenomenon, (p. 165) may occur. Heart block with a 2:1 ratio may occur if large amounts of digitalis have been used to terminate the rhythm in the presence of heart failure. This form of the tachycardia occurs as a toxic effect of digitoxin (Fig 24 C).

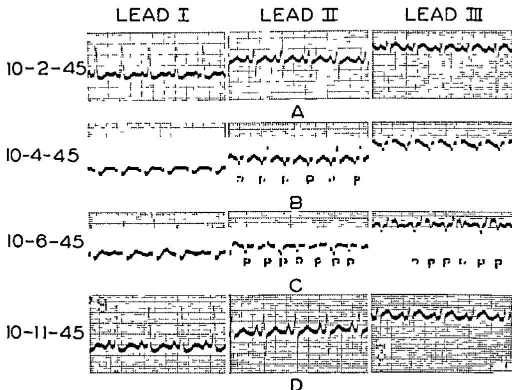


FIG 24

Electrocardiograms of a Woman 33 Years of Age with Auricular Paroxysmal Tachycardia as a Toxic Manifestation of Digitoxin

A, taken on October 2, 1945, showed normal sinus rhythm

B, taken on October 4, 1945, showed auricular paroxysmal tachycardia at 136 per minute The P-R time was 0 12 second in Lead II The P waves were diphasic in I, negative in II and III The ectopic nature of this rhythm is apparent on comparison with the three standard leads in A

C, taken on October 6, 1945, showed auricular paroxysmal tachycardia with occasional 1 1 sequences but usually with 2 1 block The auricular rate was 200 per minute The P-R time was now

Auricular paroxysmal tachycardia is more common in younger persons than is the ventricular type. It occurs without organic heart disease and may be precipitated by excessive smoking or alcohol, or by gastrointestinal upsets. It occurs in acute infections, acute rheumatic fever, mitral stenosis, Graves' disease, myocardial infarction, and during pregnancy

Attacks may be of short duration and require no treatment, or they may be of such long duration that termination is required (Fig. 23) because of symptoms or of the appearance of signs of impaired circulation or because the circumstances under which attacks occur (as in the presence of coronary occlusion or mitral stenosis) make early restoration of normal rhythm urgent When they occur

in patients without apparent organic heart disease the consequences, unless the attacks are prolonged, need not cause concern. The rhythm is very ineffective, being associated with decrease in cardiac output per minute and per beat, prolongation of the circulation time, and dilatation of the heart (Stewart and associates)

Treatment

OBJECTIVES There are two objectives of treatment: first, to stop the present attack, second, to prevent other attacks from occurring. When they occur in patients with the *Wolff-Parkinson-White syndrome (short P-R—long QRS* syndrome) (see pp. 168–169) they may be difficult to terminate. The measures which are effective in stopping auricular paroxysmal tachycardia usually are effective also in auriculoventricular paroxysmal tachycardia.

PROCEDURES. Patients may be greatly disturbed by the first attack but become accustomed to recurrences They should be reassured. They should be quiet, and should be lying down when drugs or mechanical measures are used, if the attack is of long duration they should remain in bed until the attack stops. If patients have discovered simple measures which have brought previous attacks to an end, these may be used first.

Attacks are usually ended by the induction of vagal or parasympathetic effects either by maneuvers or by drugs

The following measures may be effective:

1. Have the patient *take a deep breath* and hold it as long as possible.
2. Have the patient expire *against the closed glottis* as in the Valsalva experiment.
3. Have the patient *inspire after closing the glottis* (Muller).
4. Have the patient *strain as at stool*
5. Bending forward from the waist with the head between the legs may be effective.
6. One patient stopped attacks by *lying down and raising the feet.*
7. The *mechanical induction of gagging* or of nausea and vomiting may be effective.
8. Ocular pressure on one eyeball and then the other is so painful that it is used *infrequently*
9. Carotid sinus pressure may abolish the attack. It is carried out with the patient lying down The patient's head is held firmly. The carotid bulb is identified in the bifurcation of the carotid artery and pressed with the thumb or third or fourth fingers against the cervical spine, first one and then, after a suitable interval of rest, the other carotid sinus is pressed for five to ten seconds (Fig. 23 *F*). If pressure on either side is not successful, pressure may be exerted simultaneously on both sides. In one case carotid sinus pressure while the patient was taking a deep breath and holding it was effective after either of the foregoing measures alone had not been successful Carotid sinus pressure should be used with extreme care, since *hemiplegia has been reported from this procedure.* It should not be carried out in older patients. Atropine 0 0006 Gm for intravenous use or 1 0 cc. of a 1:1000 solution of adrenalin for hypodermic injection should be ready in a

syringe before pressure is started so that it can be administered quickly if asystole is of long duration. It is recalled that what was formerly spoken of as "vagus pressure" in the neck was in fact carotid sinus pressure, pressure on an exposed vagus nerve does not induce slowing of the heart rate *Patients should not be taught the procedure of carotid sinus pressure*, if it is expedient under certain circumstances, it may be taught to a member of the family.

10. *Digitalis* has been the drug of choice and the one most commonly effective in our experience. If the manipulatory measures have not been effective and the paroxysm has been of several hours' duration the patient should be put to bed and digitalized rapidly (see pp 70–72 and 144) Digitalis may be used in the form of whole leaf, 1.8 Gm being given in 24 hours if the patient has not had the drug within two to three weeks (Fig 23 *H* and *I*)

If there is urgency *lanatoside C* 1.6 mg may be given intravenously if the patient has not had any digitalis within two or three weeks (p 77), or ouabain may be prescribed in the usual amounts (p 77) If one of these preparations for intravenous use is not available, and if the patient is nauseated and vomiting and cannot take digitalis orally, *digitoxin* 1 2 mg may be given intravenously at once provided it is certain that digitalis has not been used recently Digitalization may be completed by giving a total of 1 8 to 2 0 mg of this drug intravenously, as nausea abates the oral route may be used It is safer to give 0.8 mg intravenously followed in three to four hours by 0 4 mg by the same route Digitoxin should be diluted with normal saline because it is dissolved in 40 per cent alcohol Lanatoside C, however, would be preferred to digitoxin if an intravenous preparation is required

When reversion to normal rhythm does not occur in the first 24 hours of oral digitalization, as it commonly does, additional amounts are given, for instance, 0.2 Gm. of the whole leaf or 0 2 mg of digitoxin two or three times a day If the clinical strength of the digitalis preparation is not known, smaller amounts are used, such as 1.5 Gm of the whole leaf in 24 hours instead of 1 8 Gm. With lanatoside C, normal rhythm may be restored within a few hours By whatever method it is carried out, reversion to normal rhythm usually occurs at some time in the course of digitalization If the drug has been pushed beyond the usual therapeutic amounts nausea and vomiting may occur Occasionally 2 1 heart block occurs, especially if heart failure is present and more than the usual amount of digitalis has been used in the effort to restore normal rhythm In other instances auricular paroxysmal tachycardia with 2 1 block has appeared to be a toxic effect of digitoxin (Fig 24 C). If the attack of auricular paroxysmal tachycardia is an *isolated* one and attacks occur infrequently, maintenance amounts of digitalis are not required after reversion to normal rhythm has occurred It is more expedient, if digitalis has been found effective, to use the drug again with each recurrence

11. The drug of choice after digitalis is *quinidine*. It may be given by mouth or intramuscularly as described in the treatment of auricular fibrillation (p 148) and ventricular paroxysmal tachycardia (p 177) Quinidine hydrochloride should be given intravenously only when other measures have failed and persistence of the paroxysm is hazardous, fatal accidents have resulted from its use by this route. Quinidine lactate is another preparation available for intravenous use (see p 177).

12 *Methacholine chloride* (formerly mecholyl chloride) (acetyl-beta-methyl-

choline chloride) subcutaneously frequently terminates this rhythm (Fig 23 C an D). The amount required increases with the age of the patient. The dose is 1 to 20 mg. in patients ten to 20 years of age; it is 30 to 50 mg. in those from 2 to 50 years. The average effective dose is about 30 mg. If it is not effective in few seconds, gentle massage of the site of injection may accelerate the effect If there is still no effect, pressure may then be made over first one and then th other carotid sinus.

It is well to have one observer listen over the precordium when methacholine chloride is used alone or with carotid sinus pressure, in order to be aware of the response of the cardiac rhythm. If an electrocardiographic apparatus is available and there is adequate assistance, a continuous record of one lead of the electro cardiogram may be taken during these procedures.

The physician should be aware of the sequence of effects of this drug. Continuous electrocardiograms (Fig 23 C and D) show that these are auriculoventricular heart block, long periods of auricular standstill with the ventricles "escaping" occasionally, and long intervals of ventricular inactivity, before reversion to normal rhythm. Only varying grades of heart block may occur with quick return to auricular paroxysmal tachycardia, or there may be reversion to normal rhythm for a few minutes, with prompt return to the auricular paroxysmal tachycardia

The side effects of the drug are dramatic and may be alarming Bronchial secretions increase with profuse expectoration; there may be bronchospasm with asthmatic breathing, vomiting, or fecal incontinence, urticarial wheals may appear. Atropine 0.0006 Gm. should be ready for intravenous use should asystole be prolonged or the side effects persistent and troublesome. If there has been a minimal effect without reversion to normal rhythm, the next higher dose of methacholine chloride may be tried after recovery from the effects of the smaller dose, which may take as long as an hour.

Methacholine chloride should not be used in patients who have a history of allergic manifestations, such as asthma and hay fever, or sensitivity to foods such as fish or strawberries.

13. Neostigmine (prostigmine) may be used to terminate attacks of auricular and of nodal paroxysmal tachycardia. Neostigmine methylsulfate 1.0 mg. is given intramuscularly, 2.0 cc. of a 1:2000 solution. Normal rhythm may be restored within five minutes, with heart block varying from prolongation of P-R interval to higher grades of block for 15 minutes or longer. The restoration of normal rhythm occurs through the vagal or parasympathetic effects of this drug.

14. Atabrine (quinacrine hydrochloride) has been used to bring about reversion of auricular fibrillation and supraventricular paroxysmal tachycardias to normal rhythm This drug is a cardiac vagal inhibitor. It is given intramuscularly in 0.3- to 0.6-Gm amounts dissolved in 10 0 cc of 1 per cent procaine solution. Reversion occurs within two and one-half hours

15. Magnesium sulfate, when given intravenously in doses of 10.0 to 20.0 cc. of a 20 to 25 per cent solution, may cause reversion to normal rhythm. Disturbance of conduction and ventricular premature contractions occur for a short time after the injection. Patients complain of a sensation of intense heat after the drug

is given. Some patients sweat and become flushed, nausea occurs, and rarely vomiting.

16. *Apomorphine*, 5.0 mg. hypodermically or *syrup of ipecac* 4.0 to 8.0 cc. by mouth may be used to induce vomiting and thereby terminate the attack. These drugs are not used often.

17. *Veratrum viride* has been used in the treatment of auricular paroxysmal tachycardia. The main actions of this drug are, slowing of the heart rate, fall in systemic blood pressure, slowing of the respiratory rate, and a "collapse reaction" characterized by sweating and fall in body temperature. The toxic side effects are nausea, vomiting, diarrhea, headache, and cardiovascular collapse. Since large doses are vomited, death from its use is rarely encountered. The site of action of the drug is believed to be the vagal nuclei in the medulla and the afferent nerve endings of the vagus nerve. Atropine will abolish the effects of veratrum and should be at hand for immediate use in the event of overdosage. Ten Craw units may be given orally as the first dose. It may be repeated at hourly intervals for three doses. Current researches on the isolation and properties of the active principles of veratrum viride may lead to wide use of this drug.

18. Youmans, Goodman, and Gould have reported the use of *neosynephrine* in the treatment of supraventricular paroxysmal tachycardia. Normal rhythm is restored within 35 to 70 seconds after rapid intravenous injection of this drug. This action is attributed to reflex cardiac inhibition elicited by rapid rise in pressure in the carotid sinuses and the aortic arch, as a result of vasoconstriction. The initial dose should not exceed 0.5 mg., with subsequent doses selected on the basis of the pressor response to the initial dose. Most attacks were reverted by 1.0 mg. or less.

I have had no experience with the use of neosynephrine for this purpose because it does not appear to me to be a safe procedure to increase the blood pressure so suddenly in patients whose circulation may already be impaired by abnormal rhythm.

19. On ordinary occasions, I do not think that *morphine* should be used to stop paroxysms of tachycardia if only for the reason that the recurrent nature of paroxysmal tachycardia may lead to addiction. Morphine 15.0 mg. hypodermically should be used only if the patient is very ill and other drugs are not available.

20. Sedatives may be effective in terminating an attack. *Phenobarbital* 30.0 mg. by mouth three times a day or *triple bromide* 1.0 Gm. three times a day may be given. Phenobarbital may be used also for its sedative effect if the patient is disturbed by the paroxysm.

21. *Pronestyl* has been effective in restoring normal rhythm in a few patients (p. 179).

A long list of drugs and measures which may be employed in terminating attacks of auricular paroxysmal tachycardia has been given. Sometimes one or more of the simple procedures (the first nine above) are effective. When they are not, the circumstances under which the attack occurs and the associated disease may determine the drug to use. I use digitalis more frequently than the other drugs, quinidine being next in order on the list. It might be necessary to try the whole armamentarium of drugs in stubborn cases before the attack is brought to an end.

Prevention of Paroxysms

It may be easier to stop a paroxysm of tachycardia than to prevent its recurrence. Patients should be encouraged to take a calm attitude about the attacks but at the same time to treat them with proper respect Emphasis is placed on previous attacks that have been terminated, and on their varying frequency. They should avoid the events which precipitate attacks if these can be distinguished: emotion, smoking, overeating, or alcohol are common examples When attacks occur patients should lie down as soon as possible. If attacks occur at intervals as long as a month or more, it is best not to give a medication continuously to prevent occurrence but to rely on stopping an attack promptly when it occurs.

DIGITALIS If attacks occur every few weeks or oftener and digitalis has been effective in stopping them, recurrences may be prevented for long periods of time by daily maintenance doses of 0.2 Gm of whole leaf or 0.15 to 0.2 mg. of digitoxin. *In the event of an attack the 24-hour dose may have to be increased. This may* result in nausea and vomiting before the attack is brought to an end. When digitalis is given over long periods of time it is good practice to take occasional electrocardiograms, especially if the clinical strength of the preparation is not known, in order to detect prolongation of the P-R time

QUINIDINE. For patients in whom quinidine has been effective but digitalis has been of no avail, as well as for those in whom digitalis stopped attacks but does not prevent recurrences, daily doses of quinidine may be of benefit *If the* initial maintenance dose of 0.2 Gm twice a day is not effective, it is increased to 0 2 Gm. three times a day. For a short period 0 2 Gm four times a day may be given but this is rarely necessary except transiently. Indeed, I do not think it wise to give large amounts such as 1 0 Gm. or more daily over long periods of time When quinidine is used in ration doses prophylactically occasional electrocardiograms should be examined for prolongation of QRS conduction time.

NEOSTIGMINE (PROSTIGMINE) When digitalis and quinidine *fail to prevent* attacks, neostigmine intramuscularly in 1 0-mg doses may stop the attack. If it is successful, ration doses of the drug may be given. It may be given as neostigmine bromide 0 015 Gm three times daily by mouth equally spaced through the day.

PROPYLTHIOURACIL I have given propylthiouracil with apparent benefit to a few patients who suffered from frequent and prolonged attacks of supraventricular paroxysmal tachycardia which did not respond to ration doses of digitalis or quinidine *(see pp. 329–330)*.

Paroxysmal Tachycardia in Infants and Children

Paroxysmal tachycardia occurs occasionally in the newborn and is not uncommon in infants during the first two or three years. The paroxysm may be of auricular or of nodal origin and a few instances of auricular flutter have been recorded The paroxysm may be difficult to terminate and if it persists may lead to heart failure The drug of choice is *digitalis* Digifoline in 0.05- to 0 1-Gm doses and digitoxin in 0 05- to 0.1-mg doses have been used. Reversion to normal rhythm may occur after 0.1 to 0.3 Gm of digifoline or appropriate doses of digitoxin As experience has now been gained with lanatoside C in supraventricular paroxysmal

tachycardia, it may be that this drug in small amounts will be useful in infants and children also. The side effects of methacholine chloride make it dangerous to use in children of this age.

Paroxysmal tachycardia occurs in *older children* and is usually supraventricular in origin, but occasionally arises in the ventricles. The onset may coincide with an acute infection and the attack may be of long duration. Mayer has reported persistent paroxysmal tachycardia in a girl 10 years old which had been present since one year of age. I have seen a boy 8 years of age in whom nodal or auricular paroxysmal tachycardia has been present at all examinations since birth

The whole range of measures in the order mentioned on pages 136–139 may be tried In the 8-year-old boy mentioned above transient reversion to normal rhythm for one or two beats with normal P-R and QRS conduction times sometimes occurred after exercise of jumping up and down Reversion to normal rhythm occurred after the use of lanatoside C intravenously The drug was given in the fol
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making a total of 1.2 mg. One-half hour afterward he experienced slight nausea Nearly four hours later (20 hours after the first injection) 0 2 mg additional was given. Twenty minutes later nausea and vomiting occurred Following this there was reversion to normal rhythm for 30 minutes. During the next few hours there were longer and longer reversions to normal rhythm until this rhythm prevailed with only occasional short runs of paroxysmal tachycardia After the patient recovered from the gastrointestinal toxic symptoms he was given the digitalis whole leaf by mouth, an attempt being made to replace the rapidly excreted lanatoside C and to provide for maintenance amounts Digitalis was chosen for this patient because it appeared to be the only practical drug that could be used over long periods of time if it turned out to be effective If digitalis fails to maintain normal rhythm over a long period of time upper thoracic sympathetic ganglionectomy (pp. 186–187) will be considered

Auricular Fibrillation

Auricular fibrillation is the most common irregularity of the heart which requires treatment either per se or because of associated heart disease or heart failure The therapeutic approach depends on whether the rhythm is paroxysmal or chronic. In the former the aim is to restore normal sinus mechanism In the latter, the optimal course most frequently is to control the ventricular rate and to refrain from attempting conversion to normal rhythm

In auricular fibrillation the normal coordinated contraction of auricles and ventricles under the direction of the sinus node is replaced by a rhythm characterized (1) by absence of rhythmic coordinated contraction of the auricles, but (2) by these chambers being dilated and distended with blood, (3) by small, irregular, ineffective twitchings over the auricular surfaces, and (4) by irregular ventricular activity. The rhythm can usually be diagnosed by physical examination It is recognized in the electrocardiogram by absence of P waves, presence of fibrillation waves, and irregular spacing of QRS complexes (Fig 7)

Instead of the usual origin and spread of the sinus stimulus, the current concept is that the excitation wave passes continuously over a circular pathway in the auricular muscle around the opening of the great veins at a high frequency of 400 to 600 per minute and with a variable pathway, so that the fibrillation waves vary in the electrocardiogram. The refractory periods of the auriculoventricular

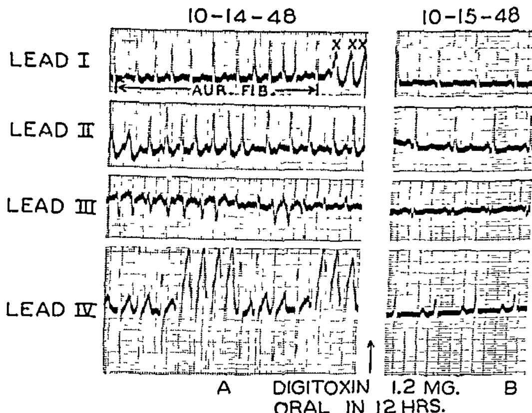


Fig 25

Reversion of Auricular Fibrillation with Ventricular Paroxysmal Tachycardia to Normal Sinus Rhythm on Digitalization with Digitoxin in a Man 69 Years of Age.

A, taken on October 14, 1948, at 8 00 P M showed auricular fibrillation with a rapid ventricular rate of 200 per minute. There were frequent runs of multiple ventricular premature contractions in all leads giving rise to short runs of paroxysmal tachycardia In Lead I these are indicated by X After this record was taken the patient was given digitoxin 1 2 mg orally in twelve hours.

B, taken at 10 05 A.M. on October 15, 1948, showed reversion to normal sinus rhythm at a rate of 68 per minute. The P-R conduction time was normal.

conducting system and the ventricles will block some of these impulses, so that the ventricular rate in untreated cases is usually rapid and irregular—generally as high as 130–150 or more per minute (Figs 7 and 25). There are occasions, however, when the spacing of the ventricular beats is regular. Auricular fibrillation with a rapid ventricular rate results in decrease in cardiac output per minute and per beat and slowing of the circulation time. The heart may dilate. If the ventricular rate is rapid there is little blood in their chambers when systole occurs, so that

contraction may not expel enough blood to form a radial pulse, thus accounting for the wide pulse deficit (Fig 5) which represents wasted energy on the part of the heart. At the next systole there will be more blood in the chambers and enough may be available to give rise to a pulse. The pulse volume varies from beat to beat. Carotid sinus pressure slows the ventricular rate transiently.

Auricular fibrillation may be chronic (Fig 7), that is to say permanent, or it may be transient, and is usually called paroxysmal The transient attacks may be for a few beats only, may be associated with change in position, or may persist for several hours. The rhythm may revert to normal spontaneously after considerable periods.

Although commonly associated with organic heart disease, auricular fibrillation may occur transiently, and occasionally permanently, without detectable cardiac pathology. It occurs transiently in active rheumatic infection, in pneumonia, myocardial infarction, and pulmonary infarction. It is of common occurrence in chronic rheumatic heart disease especially when mitral stenosis is present It occurs less frequently in hypertensive, arteriosclerotic, syphilitic, and congenital heart diseases. It occurs in chronic constrictive pericarditis, occasionally in diphtheria, and very rarely in subacute bacterial endocarditis It is a frequent complication of Graves' disease In organic heart disease the rhythm is commonly associated with congestive heart failure, in fact its onset may precipitate cardiac decompensation

Treatment of Chronic Auricular Fibrillation

There are a few patients who present a slow ventricular rate which increases only moderately with exercise and who have no evidence of organic heart disease No special treatment is required for these patients They should be told about the rhythm, and should be examined occasionally and told to report at once any change in functional capacity or the appearance of symptoms There are a few patients even with mitral stenosis or arteriosclerotic heart disease who do not require therapy since they fulfill the requirements mentioned above The use of quinidine in this group of patients is discussed on page 148 On the other hand most patients exhibiting this rhythm require treatment not only of the rhythm but also of the accompanying heart failure In certain instances moreover decision must be made whether to attempt conversion of the rhythm to normal sinus mechanism.

ACTION OF DIGITALIS IN AURICULAR FIBRILLATION Digitalis achieves its dramatic effect in auricular fibrillation by increasing the auriculoventricular block. Fewer of the excitations from the circus motion in the auricles therefore pass down to the ventricles The interval between each heart beat is longer and the ventricles contain more blood before each contraction. Therefore each stroke volume is greater. As slowing occurs the discrepancy between the apex rate and the radial rate decreases, and indeed the pulse deficit may be abolished If the drug is pushed beyond the therapeutic level, complete heart block may occur None of the impulses pass down the auriculoventricular conduction system to the ventricles, which beat under the influence of the idioventricular center and assume their independent rhythm (Fig 31 I) Atropine abolishes the vagal effect of digitalis and causes a rise in the ventricular rate.

Additional results of digitalization are that the dilated heart becomes smaller, *the extent of ventricular contraction* is augmented, and the auricular pressure falls. These additive effects result in increase in volume output of the heart (Fig. 17).

If the ventricular rate is rapid the patient should be put at rest in bed until the rate is retarded by digitalis. Bed rest should be required if the patient has evidence of heart failure. Before digitalis is given it should be made certain whether the patient has had any of the drug within the preceding two to three weeks. When *heart failure is present digitalis usually* exerts a beneficial effect and may provide adequate diuresis to free the patient of congestive manifestations (p. 11).

WHOLE LEAF. If the patient is in bed and has not had digitalis within two to three weeks, digitalization may be undertaken rapidly in 24 hours by giving 1.8 Gm. of the powdered *whole leaf* (U.S.P. XIV). It appears that 1.8 Gm. when given in 24 hours to most patients with auricular fibrillation with a rapid ventricular rate will slow the ventricular rate to around 70 to 75 per minute without nausea and vomiting (Figs. 5 and 7). It may be called the *digitalizing amount*. Experience has also shown that the amount is essentially the same for all patients irrespective of body weight. Excretion during the first 24 hours can be neglected or at most can make only the difference of one maintenance dose.

Any of the well-known preparations of whole leaf may be used and standardized. If 1.8 Gm. is the digitalizing amount of the preparation it may be given as follows: 0.8 Gm. as the first dose, 0.5 Gm. four to five hours later; 0.3 Gm. four to five hours later, and 0.2 Gm. four to five hours later still. Additional amounts are given in the second 24 hours to achieve adequate slowing. If the clinical strength of the preparation is not known smaller amounts of the drug are used. Successive doses are not given if nausea, vomiting, or ventricular premature contractions appear or *if the ventricular rate falls to 60 beats per minute or lower. Simultaneous* ventricular and radial pulse rates are counted frequently and before each dose to ascertain the ventricular slowing and the pulse deficit.

Full therapeutic digitalization should be accomplished without nausea and vomiting or other toxic signs, which, along with ventricular premature contractions, may be present as manifestations of heart failure, yet disappear with digitalization and improvement in the patient's cardiac status.

DIGITOXIN. It is the common experience that when *digitoxin* is used 1.8 to 2.0 mg. is required in order to achieve adequate slowing of the ventricular rate if it is given in 24 hours. The same schedule as that recommended for the whole leaf can be followed, substituting milligrams for grams. An adequate amount of digitoxin to achieve *satisfactory slowing of the ventricular rate is more likely to cause* toxic symptoms than the whole leaf. It is therefore a less satisfactory drug to use for routine digitalization. Since 1.2 mg. is adequate to digitalize only a very few patients, the infrequency of toxic effects which is claimed by those who recommend this amount is accounted for by the inadequacy of the dose.

If the patient is nauseated and is vomiting and digitalis cannot be given orally, digitoxin may be given intravenously in the same amounts and according to the same schedule as given by mouth. But it might be more appropriate to use one

of the other glycosides. If digitoxin is to be given intravenously it should be definitely established that the patient has not had digitalis in three weeks or longer. The injection of 1.2 mg. intravenously in a single dose is not without danger, and I do not subscribe to its use, although it has been widely advocated. In our studies of the effect of digitoxin orally and intravenously in an effort to arrive at the digitalizing amount, we did not encounter serious toxicity, but we have been careful to emphasize that we do not recommend this as a routine procedure. Digitoxin *should be diluted* with normal saline because it is dissolved in 40 per cent alcohol. One cubic centimeter of the solution is equivalent to 0.2 mg It has been shown *that digitoxin by mouth induces its effect at about the same time* as does the whole leaf; when it is given intravenously, its initial effects may appear sooner but its maximal effect is generally no quicker

If the need for speedy digitalization is urgent either ouabain 0.5 mg., or lanatoside C 1 6 mg, may be given intravenously followed later by oral digitalis. We have found lanatoside C a very useful drug It can be given intravenously Its effects are apparent within a few minutes, its maximal effect in two to three hours It is excreted within 36 to 48 hours.

Digitalis may be given by rectum as a micro-enema if there is nausea and vomiting and if none of the preparations which have been mentioned are available

MAINTENANCE OR RATION DOSES. With the ventricular rate slowed to the optimal level of around 70 per minute, ration doses of digitalis should be given daily for maintenance of this range Experience has shown that a resting ventricular rate of around 70 per minute is optimal Moderate activity will increase the rate to the neighborhood of 100 to 110 per minute If the resting rate is higher than the normal, perhaps 90 to 100, the rate with activity is even greater, to perhaps 120 to 140 per minute The ventricular rate is an excellent guide to the amount of digitalis required If the patient is in the hospital or at home under observation after digitalization the dose given each day can be varied to maintain the rate at 70 per minute.

The average daily maintenance ration is obtained if the total amount given for maintenance over a number of days is divided by the number of days of observation. The average maintenance dose of digitalis for many patients requiring the drug is 0.2 Gm a day, other patients require 0 2 Gm. one day alternating with 0 1 Gm the next, in short, 0 15 Gm daily; others require as little as 0.1 Gm , and fewer still 0 1 Gm. every other day A few patients require more than the amounts mentioned When digitoxin is used the average daily maintenance amount is approximately 0.15 mg , a few patients require 0 2 mg or more daily, some as little as 0 1 mg or less. If, however, 0 2 mg is given to all patients—the procedure which has been advocated by some writers on the subject—accumulation finally occurs with nausea, vomiting, prolongation of conduction time, abnormalities of rhythm, and other toxic manifestations in a large number of patients The rate of dissipation is slow and toxic signs may persist for several days after the drug is discontinued, the toxic signs persist longer than after intoxication from the whole leaf.

The question of conversion of auricular fibrillation after digitalization to normal rhythm by the use of quinidine is discussed on page 147.

AMBULATORY DIGITALIZATION. It is often possible to digitalize a patient with auricular fibrillation while ambulatory. The principles of this method and a tabulation of a sample schedule are given on page 95.

The patient is given written directions for taking the drug, and is warned not to continue with the schedule if nausea or vomiting occur. If these symptoms occur and the schedule is interrupted, the dosage is later resumed at this point. Account is kept by the patient of the amount taken each day, and reported to the physician at the next visit. If the patient has had no digitalis in recent weeks the earlier amounts in the above schedule would not be expected to cause toxic symptoms and therefore the doses may be larger. Toward the end of the week when full therapeutic digitalization is being approached, the amounts prescribed are smaller.

DIGITALIS TOXICITY. Signs of toxicity such as nausea and vomiting, loss of appetite, ventricular premature contractions, yellow vision, excessive slowing of the ventricular rate, and complete heart block should be looked for. Complete heart block may supervene without nausea and vomiting If the early, more benign symptoms are detected the later more serious ones can frequently be prevented

When nausea and vomiting appear during use of the whole leaf, the drug may be discontinued until the symptoms have disappeared and then resumed; it may be sufficient, however, only to reduce the maintenance dose Similar management of ventricular premature contractions due to digitalis may be carried out. When complete heart block appears, digitalis should be discontinued until a ventricular rate of around 70 per minute has been restored. In such a circumstance a lower daily maintenance level of the drug is advised. Commonly the toxic effects of the whole leaf disappear promptly as the drug is eliminated

When toxicity occurs because of digitoxin the drug should be discontinued until the symptoms and signs have disappeared Toxicity may persist for one week or longer Batterman and DeGraff have pointed out the slow rate of dissipation of digitoxin When toxicity occurs from digitoxin it is our policy to change to the whole leaf

When the ventricular rate has become too slow following the use of a digitalis preparation or when other toxic manifestations such as nausea and vomiting have appeared, the drug should be temporarily discontinued. The ventricular rate may remain slow for many days after nausea and vomiting have passed off, and then rise suddenly. This sequence of events may be avoided by restoring the maintenance amounts after nausea and vomiting have ceased and while the ventricular rate is within the optimal range. It is not uncommon for the patient to be sent home from the hospital in this interval without digitalis and without directions to take the drug later. Shortly all the drug is excreted, the ventricular rate rises, and heart failure recurs. All the benefit which resulted from hospitalization has been lost. Bed rest and hospitalization may be required again immediately. Most patients with auricular fibrillation should be continued on maintenance doses of digitalis even though the ration amount which is required is small.

The use of digitalis in auricular fibrillation occurring in hyperthyroidism will be discussed in Chapter 14 When a patient with chronic auricular fibrillation is being adequately carried on with maintenance doses of digitalis and the maintenance

should be suspected. In patients with rheumatic heart disease activity of the rheumatic infection should also be considered

Digitalis should be used in the customary manner when auricular fibrillation occurs as a complication in coronary occlusion Caution is necessary when digitalization is needed around the tenth day after infarction because the more vigorous action of the heart under the influence of the drug may cause the organ to rupture This risk, however, must be taken if heart failure arises.

QUINIDINE TO RESTORE NORMAL RHYTHM. Every case of established auricular fibrillation requires a decision whether to allow the rhythm to persist and to control the ventricular rate with digitalis or to attempt restoration to normal sinus mechanism Quinidine affects transition in a large number of the patients in whom its use is indicated Normal sinus rhythm is a more effective rhythm than auricular fibrillation. On the other hand the ventricular rate is more readily controlled with digitalis in the presence of auricular fibrillation than when regular sinus rhythm prevails The decision to use quinidine must be based on the indications for reversion with the knowledge that there are certain dangers underlying the use of quinidine as a drug, as well as certain ones inherent in the transition of the irregular rhythm to a regular one—no matter under what circumstances it occurs.

Quinidine restores normal rhythm in auricular fibrillation by increasing the refractory period of auricular muscle, thus breaking the circus motion when the wave coursing around the opening of the great veins reaches the area of tissue whose recovery from the previous wave has been slowed The sinus node takes over pacemaking again. Quinidine also has a contrary effect in speeding the conduction of the excitation wave, which would perpetuate the circus movement. When the effect on the refractory period is greater than the effect on conduction, normal rhythm is restored

Wégria has studied the *intensity and duration of action* of quinidine sulfate in auricular fibrillation and auricular flutter He found that the maximal effect on the rate of the circus movement was a slowing observed two to four hours after a single dose of 0.4 to 0.8 Gm. The degree of fall in the circus rate varied in different patients and was not in proportion to the size of the dose At times the effect on slowing persisted as long as ten hours After doses of 0.4 Gm every two hours for three to four days the maximal effect was only slightly greater than after a single dose of 0.8 Gm. and the peak occurred later, usually two to four hours after the last divided dose.

Yount *et al.* found that reversion to normal rhythm occurred when the mean plasma concentration of quinidine was 9.1 mg per liter When quinidine was discontinued the plasma concentration fell sharply at the end of 24 hours and showed almost no quinidine at the end of 36 hours

Conversion to normal rhythm is considered under the following circumstances

1 Conversion may be attempted if auricular fibrillation has been of short duration, in terms of months. If it has been of long duration mural thrombi may have formed in the stagnant blood in the auricular appendage and in the trabeculae of the auricular muscle and will be liable to be dislodged when the heart begins to beat regularly under the direction of the sinus node.

2. Reversion may be attempted in patients who have not suffered attacks of heart

failure and do not have evidences of congestion at the time conversion is attempted. It is known that heart failure encourages the formation of mural thrombi. If heart failure is recent, consideration may be given to the restoration of compensation before attempting reversion

3 Conversion may be attempted if the heart is not unduly enlarged. It is known that mural thrombi as a source of emboli are more likely to form in large, dilated hearts.

In deciding about conversion to normal rhythm consideration should be given to the observation that some patients manage better with auricular fibrillation than with normal rhythm because the ventricular rate is more easily controlled.

Reversion of chronic auricular fibrillation to normal rhythm by the use of quinidine is attempted infrequently by experienced physicians. There have been recent reports, however, advocating reversion more frequently even though heart *failure is present and there are other contraindications* *Although statistics on the* subject are inadequate it appears that reversion to normal rhythm does not seem to increase the incidence of emboli Many physicians think this eventuality should not prevent the use of quinidine There has been one unusual case report relating the continuous elaboration of embolic material into the blood stream over long periods of time in a patient with auricular fibrillation. These phenomena ceased with conversion of the rhythm to normal sinus mechanism with quinidine.

It was stated earlier that quinidine should not be used in the presence of *congestive heart failure* Although Askey has pointed out that sudden death is a hazard in the use of quinidine in auricular fibrillation in the presence of congestive heart failure, he inferred that the increased risk was justified owing to the risk of the heart disease itself Evidence for this consisted in the improvement of heart failure on restoration of normal sinus rhythm In another recent report large doses of quinidine were given to cause reversion to normal rhythm and large ration doses were required to maintain it. Since many of the patients died within short periods of institution of this therapy, it still does not appear to me to be a safe course.

When quinidine is being given observations should be made to detect the *following* untoward events: (1) Prolongation of the QRS time in the electrocardiogram, (2) ventricular premature contractions and their increase in number; (3) a rapid regular rhythm suggesting the complication of ventricular paroxysmal tachycardia; (4) a transient, rapid, irregular rhythm during which the pulse cannot be detected, *suggesting the occurrence of ventricular fibrillation*, and (5) auricular standstill due to poisoning of the sinus node.

Quinidine and digitalis should not be given simultaneously. Combined use of the two drugs may cause ventricular premature contractions leading to ventricular paroxysmal tachycardia with alternation of origin in the two ventricles This sequence of events is usually fatal Quinidine may be given without digitalizing first if heart failure is absent and if the ventricular rate is slow

The patient should be at rest in bed. The ventricular rate is slowed first by digitalis to 70 beats a minute This drug is then discontinued and a test dose of 0.2 Gm quinidine sulfate given by mouth. *Idiosyncrasy* would be manifested by gastrointestinal upset, nausea and vomiting, diarrhea, ringing in ears, deafness, rash, fever, *ventricular premature contractions*, intraventricular heart block, throm-

bopenic purpura, or exfoliative dermatitis If it is urgently necessary to use quinidine, as it may be in the presence of ventricular paroxysmal tachycardia, the test dose may be eliminated and the risk of idiosyncrasy assumed When there is no urgency it does not appear wise to omit the test dose even though idiosyncrasy is not common.

If evidences of sensitivity do not appear within two to three hours, the following regimen may be instituted. 0 4 Gm is ordered four times a day at four-hour intervals. If reversion does not occur the first day it is increased to 0 4 Gm five times at the same intervals the next day, and to six times the following day. Reversion may be imminent when the ventricular rate slows. If reversion has not occurred after the third day, quinidine is discontinued and the ventricular rate is slowed again to around 70 beats per minute by digitalis Another course of quinidine may then be instituted If larger amounts are given, special attention should be given to the occurrence of ventricular premature contractions, and to sudden increase in the heart rate suggesting the onset of ventricular paroxysmal tachycardia. Electrocardiograms should be taken to detect increase in QRS conduction time. Quinidine 0 2 Gm. may be given twice a day for several days as the maintenance amount after reversion to normal rhythm in order to prevent recurrence of auricular fibrillation

Should auricular fibrillation recur while the patient is on quinidine another attempt at restoration is not made unless maintenance of normal rhythm appears to be essential If auricular fibrillation recurs after the patient has been off quinidine for a few days and there appear to be good reasons for restoration of normal rhythm, another trial may be made Maintenance doses of quinidine should be kept up for a few days longer than the first time if reversion occurs Quinidine should not be given daily in ration amounts to patients over a long period of time. Thrombopenic purpura has been recorded following the use of quinidine In a susceptible individual fall in platelets with bleeding occurred after as small an amount as 0 1 Gm of the drug had been administered for the purpose of proving implication of quinidine as the offending agent

Occasionally in both chronic and paroxysmal auricular fibrillation when quinidine is being given, the rhythm is converted to auricular flutter which cannot be changed either to normal rhythm or auricular fibrillation by large amounts of quinidine or digitalis.

The recent report of Yount et al. is of interest They recommend the following dose schedule quinidine 0 2 Gm every 4 hours day and night, increasing by 0 1 Gm. per dose at the end of each 24- or 48-hour period In their series reversion occurred on the average after 6 days on a mean dose of 0 42 Gm. every 4 hours The duration and severity of the disease did not influence the result The oldest patients responded most readily and on the smallest doses After reversion they continued the same doses for 24 to 48 hours, when the schedule was changed to 6-hour intervals, and later further reduced The average maintenance on the 6-hour schedule was one-half that necessary for reversion When on the 4-hourly schedule the 4 A.M dose may be omitted if it is added to the midnight dose in the enteric coated form, which has its peak of absorption 5 to 6 hours after ingestion.

From observations of Alexander and his associates, it appears that *synthetic*

quinidine sulfate and *dihydroquinidine* can be used as safe and effective *substitutes* for commercial (U.S.P.) quinidine in the treatment of cardiac irregularities. Synthetic and commercial quinidine have similar durations of action.

Recently two reports have appeared on the use of *fagarine*, an alkaloid derived from the Argentine plant *Fagaracoco*, as a substitute for quinidine. Deulofeu and Taquini have found that normal sinus rhythm in 6 patients with auricular fibrillation and auricular flutter was restored within 30 minutes after a single intramuscular dose of 0.06 to 0.12 Gm. of fagarine hydrochloride. Scherf, Silver, and Weinberg have used alpha-fagarine hydrochloride in patients with auricular fibrillation. In 6 of 13 patients normal rhythm was restored. In 2 patients fatal ventricular fibrillation appeared, and in 5 others multifocal ventricular premature contractions were observed. These toxic effects prevent the use of the drug for clinical purposes.

Recently Gertler and Yohalem have reported the reversion of auricular fibrillation to normal rhythm by the use of *atabrine*, as a substitute for quinidine. They gave 0.6 Gm. in 10.0 cc. of 1 per cent procaine intramuscularly. Return to normal rhythm occurred in two and one-half hours. The blood level of atabrine reaches a maximum in around one hour, and the maximal effect should occur early.

PRONESTYL TO RESTORE NORMAL RHYTHM. This drug is occasionally effective in restoring normal rhythm (p. 179).

Anticoagulants

Prolonged anticoagulant therapy has been recommended in the treatment and prevention of embolic phenomena in chronic auricular fibrillation, especially in patients with mitral stenosis (Chapter 4). Ration doses of dicumarol are given depending on the prothrombin time. Patients under this therapy have not been followed long enough to establish its efficacy in the prevention of embolic phenomena and whether its benefits are adequate to warrant the risks inherent in prolonged anticoagulant therapy and the frequent blood examinations which are required. Anticoagulants have been used in a few patients with chronic auricular fibrillation *before and during* the attempts to restore normal rhythm with quinidine, in order to prevent embolic phenomena. Until additional studies have been made this regimen should be undertaken only with a full realization of the dangers involved. The experience has not been sufficient to decide whether it will prove consistently to be a safe plan of therapy.

Treatment of Paroxysmal Auricular Fibrillation

The treatment of paroxysmal auricular fibrillation depends on the circumstances under which attacks occur, their duration, and the rapidity of the ventricular rate. If paroxysms are infrequent and brief, especially in a patient otherwise well and without organic heart disease, specific treatment may not be required, as the attack may stop shortly of its own accord. If they recur frequently *preventive treatment* may be indicated. On the other hand measures should be instituted promptly to slow the ventricular rate and if possible to end attacks occurring in patients suffering from myocardial infarction, pneumonia, mitral stenosis, during operations, and postoperatively—to mention a few instances—for it is not known

how long attacks may last and the onset and persistence of the rapid rate may precipitate heart failure.

Usually if the attack has been present for some hours, if the ventricular rate is rapid, if the patient is uncomfortable, and if signs of failure are present or begin to appear with or without pre-existing organic heart disease, measures should be instituted to control the rhythm. The patient while at rest in bed should be digitalized as described under chronic auricular fibrillation (p. 144). The type of digitalis is selected according to the urgency of the situation. If normal rhythm is restored during digitalization (Fig. 25), as frequently happens, the drug is discontinued On the other hand, if auricular fibrillation persists after the ventricular rate has been retarded and the signs of heart failure have been dissipated, the use of quinidine should be considered. The plan of therapy has been discussed in the section on chronic auricular fibrillation (p. 147).

Prevention of Attacks of Paroxysmal Auricular Fibrillation

Avoidance of the precipitating factors may be sufficient to prevent the occurrence of paroxysmal auricular fibrillation Among these factors are excessive alcohol intake, or a combination of late hours, smoking, and alcohol Should the patient have repeated attacks of paroxysmal auricular fibrillation and if quinidine or digitalis has been effective, he should be directed to take that drug promptly when attacks recur, in order not to delay the conversion to normal rhythm.

It does not appear expedient to give either digitalis or quinidine in ration doses continuously over long periods of time to prevent recurrence of infrequent paroxysms. Each attack should be treated when it occurs. Quinidine in ration amounts may prevent attacks when they occur frequently. When the drug is used for this purpose, occasional observation should be made to prevent toxic effects and to detect prolongation of the QRS time in the electrocardiogram (p 148). If large amounts of quinidine are required the best plan usually is to allow auricular fibrillation to continue, and to control the ventricular rate with digitalis In certain patients ration doses of digitalis may prevent the occurrence of paroxysmal auricular fibrillation when quinidine has been ineffective There is no sound basis for not using digitalis in the presence of paroxysmal auricular fibrillation The notion that it "fixes" the rhythm is without basis

Auricular Flutter

In auricular flutter the auricles beat regularly at a rate of between 200 to 400 times a minute—commonly around 300 Auricular flutter, according to the circus motion idea, is due to the excitation wave coursing in a fixed pathway around the opening of the great veins The pathway is fixed and only one excitation is given off with each circuit, so that the auricular sequence is regular Regularly spaced flutter waves slower than the "f" waves in auricular fibrillation are seen in electrocardiograms They have a saw-toothed configuration As the excitation waves spread through the auricular muscle and down the auriculoventricular system, the auriculoventricular system may not transmit them all and the ventricles may not respond to all In short, auriculoventricular block occurs. In untreated cases it is common for only half of the excitations to result in ventricular contractions, so that 2.1 heart block is present or 2 1 auricular flutter prevails (Fig. 26). The degree

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spaces to the right and left of the sternum, as well as esophageal leads, are devices which may demonstrate flutter waves when they are small or not readily apparent in the three standard leads of the electrocardiogram.

Prinzmetal and his co-workers have recently questioned not only the accuracy of the circus motion concept of Garrey and of Mines as an explanation of auricular flutter and auricular fibrillation, but also the experimental evidence which Lewis collected to support this hypothesis They think their data show that contractions spread in all directions simultaneously from a focus when auricular flutter is induced by placing aconitine in the center of the surface of the right auricle They advance the notion that auricular flutter and auricular paroxysmal tachycardia are similar mechanisms, the rate of excitation in the former being more rapid than in the latter, and in auricular fibrillation being still more rapid. There has not yet been opportunity for confirmation of these observations by others

Other investigators, especially Evans, also regard auricular flutter and auricular paroxysmal tachycardia as the same rhythm and think that auricular paroxysmal tachycardia is the essential mechanism The configuration of the electrocardiogram in typical examples of each of these, the differences the two rhythms exhibit in their response to drugs; and the passage of auricular flutter—but, in my experience, not of auricular paroxysmal tachycardia—through the stage of auricular fibrillation in the course of reversion to normal rhythm make it advantageous clinically for the present to look upon them as two different rhythms

Impure flutter is intermediate between auricular flutter and auricular fibrillation, having some of the features of both In electrocardiograms the waves corresponding to auricular activity ("fff") are not quite equally spaced as in auricular flutter Moreover they occur more rapidly, transitions to typical auricular fibrillation are recorded, the ventricular sequence is irregular This rhythm is treated in the same manner as auricular fibrillation

Auricular flutter is more commonly transient than chronic. It is usually associated with organic heart disease It occurs in the presence of chronic rheumatic valvular disease, especially mitral stenosis, in hypertension, in arteriosclerotic heart disease, and in hyperthyroidism It may be recorded in active rheumatic carditis

When it is of short duration therapy is not necessary. The circumstances under which it usually occurs, however, require its termination as soon as possible It is an inefficient rhythm, with the cardiac output per minute and per beat greatly decreased The circulation time is prolonged and the heart may dilate The venous pressure may rise Reversion to normal rhythm is accompanied by restoration of these values toward normal levels or to those pertaining before the onset of auricular flutter

Treatment

The objective in treating auricular flutter is to restore normal rhythm The patient should be in bed when this is attempted

DIGITALIS Digitalis is the drug of choice if the ventricular rate is rapid. If there is urgency, lanatoside C may be given intravenously Otherwise the whole leaf may be used It is given as described in auricular fibrillation (p 144). As the drug takes effect, the ventricular rate decreases due to the increase in auriculoventricular block; 2:1 block increases so that 3:1 and 4:1 ratios prevail. As slowing

of block is, however, very variable There may be 1:1 ratio if the ventricles respond to every auricular excitation. After digitalis the ratio may be 3:1, 4:1, 5:1 or more, or the ratio may change, causing the ventricular sequence to be irregular. Occasionally auricular flutter with 4:1 or 5:1 block occurs without digitalis especially in

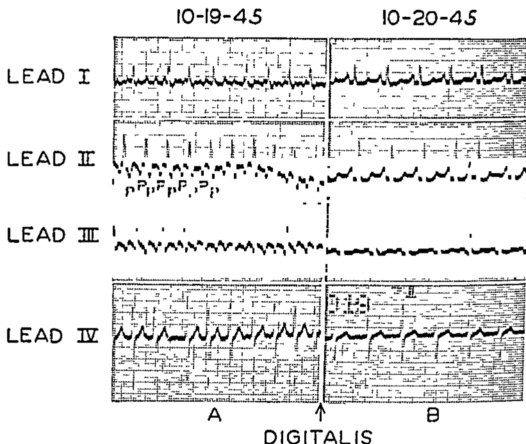


Fig. 26.

Reversion of Auricular Flutter to Normal Rhythm on the Exhibition of Digitalis in a Man 55 Years of Age

A, taken October 19, 1945, showed 2:1 to 3:1 auricular flutter Auricular rate was 352 per minute. Ventricular rate was 176 in Lead II in which 2:1 block was present but was 160 in Lead III, where ... 1 block. Flutter

... on October 19, ... nute There was

patients with arteriosclerotic heart disease. When flutter waves are seen in the jugular veins or auricular contractions are heard over the auricles, and a ratio is calculated between these and ventricular systole, auricular flutter can usually be diagnosed on physical examination If the rhythm cannot be confirmed by an electrocardiogram, appropriate therapy is instituted without it Loosening the galvanometer string so that a 2-cm. deflection equals 1 millivolt, and recording precordial derivations over the region of the auricles in the third or fourth inter-

intramuscularly. It should not be used intravenously except in extreme urgency. The use of quinidine lactate intravenously is not without danger. An instance of conversion of 2:1 auricular flutter to 1:1 auricular flutter with an intraventricular conduction defect and shock has been reported from the intravenous injection of 0.65 Gm quinidine lactate. If quinidine is effective in restoring normal rhythm, maintenance amounts should be given for a few days Its action in breaking up the circus motion in auricular flutter is the same as in auricular fibrillation.

FAGARINE The use of this new drug does not appear to have a place any more secure in the treatment of auricular flutter than early tests indicate that it has in auricular fibrillation (p. 150).

LANATOSIDE C AND QUINIDINE. The combined use of these two drugs has been recommended for the abolition of established auricular flutter Tandowsky, Oyster, and Silverglade found that giving lanatoside C intravenously increased the auriculoventricular block, thereby slowing the ventricular rate, and then converted auricular flutter to auricular fibrillation in a number of patients. These events were recorded in electrocardiograms. In a few patients normal sinus rhythm was restored one hour after digitalization With the onset of auricular fibrillation digitalis was continued by those investigators and in addition quinidine was given to restore normal rhythm On restoration of normal rhythm quinidine was discontinued but digitalis was maintained. They gave lanatoside C 1.6 mg. intravenously followed by 0.1 to 0.2 mg daily Quinidine was given in a total dosage of 1.2 to 2.4 Gm daily Normal rhythm ensued in from 12 hours to ten days after starting quinidine Caution must be exercised in the use of digitalis and quinidine at the same time in order not to induce ventricular paroxysmal tachycardia with alternation of beats in the two ventricles

PRONESTYL This drug has been effective in restoring normal rhythm in a few instances (p. 179).

CAROTID SINUS PRESSURE. This procedure increases the block in auricular flutter as well as in auricular fibrillation and thereby slows the ventricular rate, but the effect is transient In my experience it has not caused reversion to normal rhythm.

METHACHOLINE CHLORIDE. This drug may increase the degree of auriculoventricular block but is not effective in the restoration of normal rhythm (p. 137).

If *paroxysms of auricular flutter* occur often, they may be prevented in many patients by digitalization followed by maintenance amounts of the drug. If quinidine is used for this purpose toxic effects should be kept in mind. There are instances of auricular flutter which do not revert to normal rhythm either on digitalization or on careful manipulation of quinidine. One must then maintain a slow ventricular rate with digitalis. The combined use of lanatoside C and quinidine may be considered for certain of these

AURICULOVENTRICULAR, NODAL, OR JUNCTIONAL IRREGULARITIES

Auriculoventricular Premature Contractions

When an abnormal stimulus arises in the auriculoventricular node or conducting system of a normal or diseased heart a premature contraction results. The excitation wave simultaneously passes upward—initiating contraction of the auricles—and downward, resulting in ventricular contraction If the origin is high in the node,

occurs the ventricular rate *may fall to 75 per minute. If the sequence is regular, it* might be erroneously thought on physical examination that normal rhythm has been resumed. An electrocardiogram may be required to establish the diagnosis. Normal rhythm may recur at any time during this first 24 hours of digitalization. If the ventricular rate is not slowed appreciably, additional amounts of digitalis may be required; 0.3 Gm. four hours after the last of the 1.8 Gm. (see Auricular Fibrillation, page 144), or 0.3 Gm. twice in the next 24 hours. This may be one occasion on which it may be necessary to give digitalis to the point of nausea and vomiting, before normal rhythm is restored. At some time after slowing of the ventricular rate to around 75 beats per minute occurs normal mechanism may be restored directly (Fig. 26), or the rhythm *may first pass through a transient period* of auricular fibrillation. Auricular fibrillation may be detected by the irregular ventricular sequence and pulse deficit, but it may be recalled that irregular ventricular sequence may also be due to auricular flutter with changing block.

If the patient's condition is satisfactory and slowing is adequate, and if normal rhythm has not been restored during digitalization, maintenance amounts of digitalis are continued until normal rhythm occurs either promptly or after several days or longer. *Digitalis does not prevent restoration of normal rhythm either* directly or when auricular fibrillation is the intermediary rhythm. After restoration of normal rhythm, digitalis is discontinued unless it is required because of heart failure. Should auricular fibrillation persist, it is more satisfactory as a permanent rhythm than auricular flutter because the ventricular rate is more easily controlled.

Auricular flutter may occasionally be converted to auricular fibrillation by digitalis, and the latter rhythm may persist. With certain of these patients quinidine *may then be used in an attempt to restore normal rhythm; in others it may* be more expedient to allow auricular fibrillation to continue

Digitalis brings about reversion of auricular flutter to normal rhythm by its vagal [illegible] on auricular [illegible] refractory [illegible] the circus, shortens the time to make a circuit, and the auricular rate increases. The direct action of digitalis on the auricular muscle lengthens its refractory period and impedes conduction, which tend to close the gap and to decrease the auricular rate.

When *digitoxin* is used as the digitalis preparation, it is given as described on page 144 and in Chapter 3 Larger amounts, however, may be required.

The onset of auricular flutter in coronary thrombosis requires prompt therapeutic action. Oxygen by tent or mask may help to offset the retardation of the circulation due to the decline in cardiac output Aminophyllin 0.24 to 0.48 Gm. intravenously and possibly one of the mercurial diuretics may be used if signs of failure should appear before full therapeutic digitalization can be achieved. Lanatoside C or ouabain may be used intravenously if there is urgency (see p. 77) Lanatoside C 1.6 mg. may be given intravenously at once. The maximal effect should be attained in two to th[illegible]

of the ventricular [illegible]

QUINIDINE. If [illegible] if further delay after digitalization does not appear safe, or if auricular fibrillation supervenes and persists, a trial may be made with quinidine as described on page 147. The drug should be given orally if possible, but if necessary it may be used

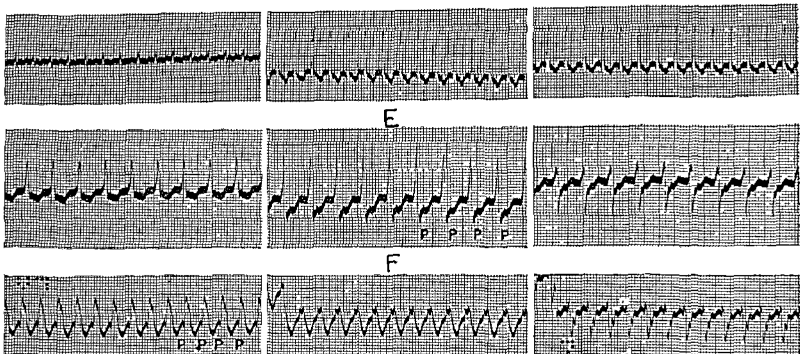


FIG 27

Examples of Auriculoventricular Paroxysmal Tachycardia

A, nodal paroxysmal tachycardia in a man 29 years of age P waves are in front of QRS complexes Rate is 150 per minute P-R time is 0 9 to 0 10 second

B, nodal paroxysmal tachycardia in a man 70 years of age P waves, concealed in QRS complexes, are not seen Site of stimulus is probably in middle of auriculoventricular conduction system so that stimulus arrives simultaneously at auricles and ventricles Rate is 180 per minute (see *Fig 28*)

C shows auriculoventricular paroxysmal tachycardia in a woman 36 years of age P waves (PPP) follow QRS complexes, indicating that stimulus arises low down in auriculoventricular conduction system, and arrives at ventricles before reaching auricles Rate is 167 per minute

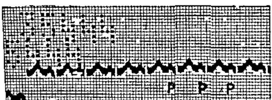
D shows an electrocardiogram of a woman 43 years of age Another instance of auriculoventricular paroxysmal tachycardia, P waves following QRS complexes Rate is 176 per minute

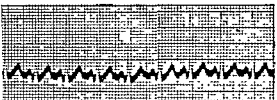
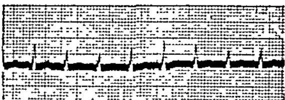
E, taken on a man 30 years of age, shows nodal paroxysmal tachycardia at the very rapid rate of 260 per minute P waves cannot be identified Stimulus presumably arises in middle of auriculoventricular conduction system

F shows another example of auriculoventricular paroxysmal tachycardia with the P waves following the QRS complexes This was derived from a man 70 years of age. Rate is 167 per minute. P waves are indicated by P

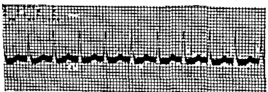
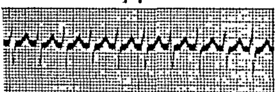
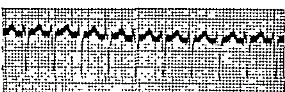
In *G* is shown an electrocardiogram of a man 49 years of age Auriculoventricular paroxysmal tachycardia is present with bundle branch block, rate being 230 per minute P waves are indicated Another interpretation might be that it is ventricular paroxysmal tachycardia Patient had many varieties of rhythms and, in the instances in which it was fairly certain that ventricular paroxysmal tachycardia was present, the QRS complexes had a different configuration

LEAD I LEAD II LEAD III

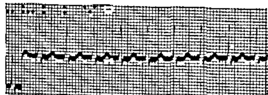
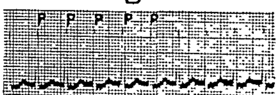


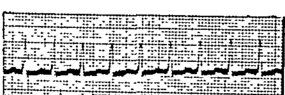



A

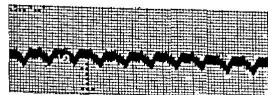
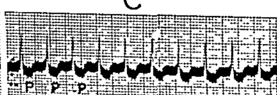




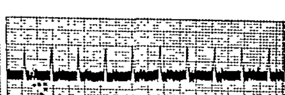
B



C



D

When premature contractions from the nodal tissue give rise to symptoms they are accorded the same therapy as that required for auricular premature contractions

AURICULOVENTRICULAR PAROXYSMAL TACHYCARDIA

Auriculoventricular paroxysmal tachycardia is a rapid, regular beating of the heart resulting from stimuli arising in the junctional tissue and is characterized by sudden onset and sudden offset. The junctional tissue controls the beating not only of the auricles, by retrograde conduction, but also of the ventricles. In electrocardiograms the P waves fall before, during, or after the QRS complexes (Figs. 27 and 28). When the P waves are in front of the QRS complexes the conduction time is 0.10 seconds or less That the P waves are concealed in the QRS complexes when the origin is near the middle of the auriculoventricular conduction system is shown in Figure 28.

Auriculoventricular paroxysmal tachycardia is more common than is generally thought It occurs in normal hearts and in hearts with organic defects. The volume output of the heart per minute and per beat is decreased, the circulation time is prolonged, and the heart may dilate.

Treatment

The treatment and the prevention of this variety of supraventricular paroxysmal tachycardia is the same as for auricular paroxysmal tachycardia (pp 136–140). Paroxysms may stop without any medication (Fig. 29 A and B, E and F). In certain instances carotid sinus pressure may be effective in restoring normal rhythm (Fig 30). Digitalis is usually the most effective drug (Fig 29 C and D) (see Pronestyl, pp 178–179). When restoration of normal rhythm is urgently required as soon as possible or when oral preparations cannot be used lanatoside C may be given intravenously (Fig 28). Attacks occurring in patients with Wolff-Parkinson-White syndrome may be difficult to revert to normal rhythm Some clinicians think that auriculoventricular paroxysmal tachycardia may be more difficult to stop than auricular paroxysmal tachycardia In general I have not been impressed that paroxysmal tachycardias occurring in a setting of organic heart disease were more refractory to treatment than when occurring in patients without heart disease

Quinidine may be effective in terminating paroxysms of nodal tachycardia. It is given in the usual doses (p 149) In patients with this irregularity Delevett and Poindexter have observed the plasma concentration of quinidine, using the Brodie colorimetric method, after a single large oral dose of quinidine sulfate. There was marked individual variation The maximal rise was reached four to five hours after administration, and varied between 1 mg and 4 mg per liter. From a study of two patients it appeared that a level of approximately 1 mg of quinidine per liter of plasma was necessary for the prevention of the tachycardia

Gertler and Yohalem found that nodal paroxysmal tachycardia which was refractory to quinidine might be successfully treated with *atabrine* In one instance normal rhythm was restored two minutes after beginning the injection of 0.1 Gm. atabrine intravenously The drug was dissolved in 10 0 cc. of normal saline The intramuscular injection of 0 4 Gm. atabrine dissolved in 10 0 cc. of 1 per cent procaine solution caused reversion to normal rhythm in another patient

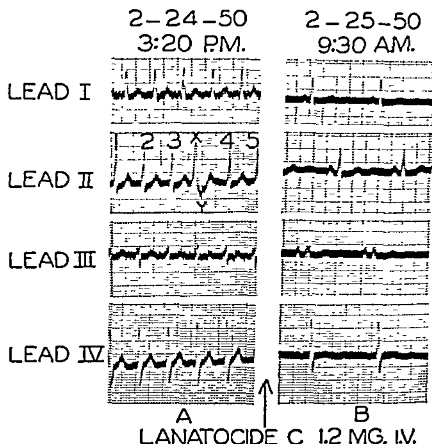


FIG. 28.

Electrocardiograms of a Man 69 Years of Age

A was taken during auriculoventricular paroxysmal tachycardia at a rate of 150 per minute. [illegible] in QRS com[illegible] contract at [illegible] 1, 2, and 3 [illegible] premature contraction. "Y" is usual P wave of auriculoventricular paroxysmal tachycardia which in other cycles is concealed in QRS complexes. Complex 4 of auriculoventricular paroxysmal tachycardia comes along at the expected time, as does Complex 5 Interval from 4 to 5 is same as two usual cycles, or same as from Complexes 1 to 3.

Record was taken at 3 20 P.M. on February 24, 1950. At 4 P.M. 0 8 mg lanatoside C was given intravenously and 0.4 mg at 10 P.M. At 9.30 A.M. on February 25 after a total of 1.2 mg of the drug intravenously, normal rhythm had been restored at a rate of 60 per minute.

the pathway to the auricles is shorter and they contract before the ventricles. In this instance P waves precede the QRS complexes in electrocardiograms. If the point of origin is near the middle of the auriculoventricular system the auricles and ventricles contract simultaneously and P waves may not be seen in electrocardio[illegible] system and closer to the ventricles, these chambers [illegible] P waves appear after the QRS complexes in electro[illegible] is 0.10 seconds or less the premature contraction is considered to arise in the upper part of the auriculoventricular tissue.

When premature contractions from the nodal tissue give rise to symptoms they are accorded the same therapy as that required for auricular premature contractions.

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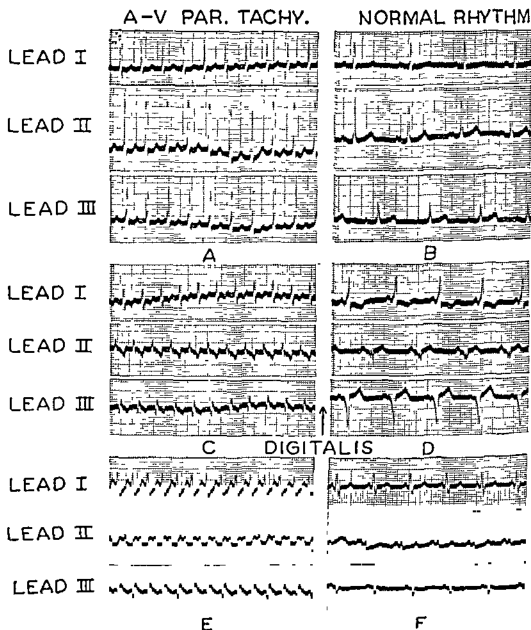


FIG 29

Methods of Treatment for Auriculoventricular Paroxysmal Tachycardia

(Caption on facing page)

Procaine amide hydrochloride has been effective in the treatment of auriculoventricular paroxysmal tachycardia. This is mentioned on pages 178-179 This may turn out to be the drug of first choice under certain circumstances.

Auriculoventricular (Nodal or Junctional) Rhythm

In this rhythm pacemaking is shifted from the sinus node to the auriculoventricular node and conduction system so that a focus in this tissue controls the contraction of both the auricles and the ventricles It is usually slower in rate than the discharge from the sinus node It may arise from one focus in this tissue or may shuttle up and down this system. In the electrocardiogram the P waves may precede, coincide with, or follow the QRS complexes, or they may move back and forth in the node from a location in front of the QRS complexes to one following them When the P waves precede the QRS complexes the conduction time is 0.10 seconds or less. Nodal rhythm is usually transient but may persist for long periods. In some patients it may recur frequently

The rhythm requires no special therapy since it does not give rise either to any symptoms or (probably) to any marked change in functional capacity of the heart. When it results from the use of digitalis, it may occur after amounts which are short of the full therapeutic doses It disappears when digitalis is discontinued Congestive heart failure which requires the use of digitalis should take precedence over the occurrence of this rhythm Atropine may cause the rhythm to disappear, even though in other patients the use of this drug seems to have caused its appearance

Wandering Pacemaker

When pacemaking shifts back and forth from the sinus node to the auriculoventricular system the rhythm is spoken of as being caused by a "wandering pacemaker" It is recognized in the electrocardiogram when the P waves shift location with respect to the QRS complexes, so that the P-R time varies The change in

A and B relate to a man 79 years of age A, taken on August 13, 1947, showed auriculoventricular paroxysmal tachycardia, with rate 167 per minute P waves appear to follow QRS com-



was prompt reversal to regular slow rhythm, as shown in D Rate 73 per minute It is apparent that patient has a short P-R, long QRS syndrome Patient had repeated attacks of auriculoventricular paroxysmal tachycardia which reverted to normal on digitalization

E, taken on a man 67 years of age, shows auriculoventricular paroxysmal tachycardia at 220 per minute Lead I shows a deformity of upstroke of QRS which is probably a P wave If this deformity were not present it might have been thought that this was an instance of ventricular paroxysmal tachycardia F shows that normal rhythm has been restored at a rate of 94 per minute Reversion occurred spontaneously In certain of the records taken during normal rhythm it appeared [illegible] nodal pa[illegible] of benefit [illegible] amounts [illegible] was required When the patient had attacks of paroxysmal tachycardia while taking quinidine, carotid sinus pressure was used to terminate them

P-R time indicates the shift of impulse formation from the sinus node to the upper part of the auriculoventricular node, down the auriculoventricular conduction system, and then on up again to the sinus node. The rhythm gives rise to no symptoms. It occurs in normal subjects. It may be transient or persistent, the latter especially in athletic subjects with a slow heart rate. It may result from digitalis or from hypersensitivity of the carotid sinuses. It does not require therapy.

DEFECTS OF THE CONDUCTION SYSTEM

"Heart block" when used without qualification usually refers to *auriculoventricular heart block*. This occurs when stimuli arising in the sino-auricular node or auricles are retarded or obstructed in their passage down the main stem of the auriculoventricular bundle. Defects in conduction after the main bundle has divided into right and left branches are known as *bundle branch block*.

Etiologic Factors

Alteration in the conduction system resulting in heart block may be brought about in several ways.

1 It may be due to structural damage from myocardial changes due to arteriosclerosis, myocardial fibrosis, myocardial infarction involving the septum, syphilitic gumma involving the conduction system, damage due to diphtheria, congenital defects especially when there is also interventricular septal defect, and possibly to rheumatic carditis and other acute infections.

2 It may be due to the toxic effect of drugs. Digitalis is not uncommonly implicated

3 Nutritional or functional changes may be the cause of heart block Uremia and myxedema may be cited as examples.

4. Vagal influences may induce blocks of all grades For instance, vagal influences may be potentiated by methacholine chloride, neostigmine, and carotid sinus stimulation. The conduction changes in rheumatic carditis may be due to vagal effects.

Duration

Heart block may be transient or permanent. When it occurs in active rheumatic carditis, during acute infections, and with drugs it is usually transient. In arteriosclerotic heart disease heart block is usually persistent and may be progressive. Rarely heart block may disappear after being present several years. The block in myocardial infarction may be transient but frequently is permanent. Heart block of the congenital variety, which is commonly high grade or complete, does not usually change or disappear. During diphtheria the degree of block may change and disappear, but once it has become stabilized it remains. The [illegible] of [illegible] ng [illegible] he [illegible] drug the patient has received, and the rate of excretion of the preparation (Fig. 11).

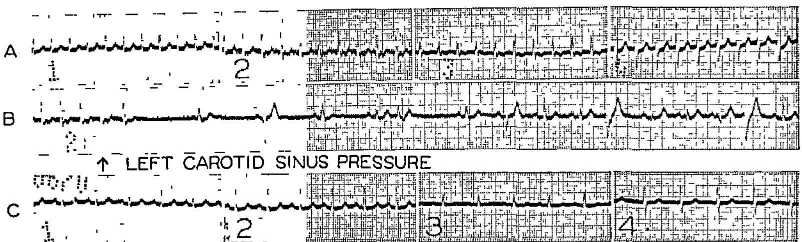


Fig 30

Reversion of Auriculoventricular Paroxysmal Tachycardia to Normal Rhythm with Carotid Sinus Pressure in a Woman 54 Years of Age.

A shows nodal paroxysmal tachycardia at 167 per minute The P waves cannot be identified and may be concealed in the QRS complexes There was induced current in Lead II

B records Lead II At the beginning of the lead auriculoventricular paroxysmal tachycardia was present At the point indicated by the arrow left carotid sinus pressure was applied, with prompt slowing of the heart rate and return to normal sinus rhythm There were different configurations of QRS complexes in certain cycles Occasional ventricular premature contractions were recorded Toward the end of this lead the rhythm was normal sinus rhythm at a rate of 100 per minute.

C, showing Leads I, II, III and IV immediately after *B* was taken, recorded normal sinus rhythm in all leads at a rate of around 100 per minute. Normal sinus rhythm persisted

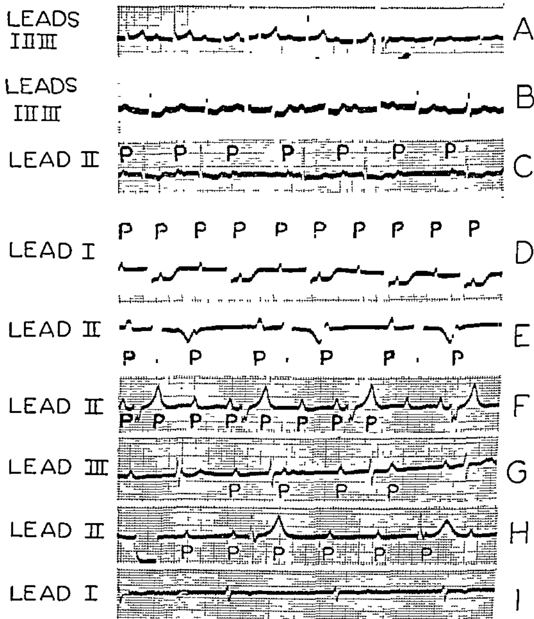


Fig 31

Various Grades of Auriculoventricular Conduction Defect (Heart Block) Due to Organic Lesions Involving the Conduction System or to Digitalis

A demonstrates first degree heart block with P R time of 0 28 second in Lead II, occurring in the course of active rheumatic carditis

lengthening of P-R time from 0 35 second in first complex to 0 41 second in second one and

Degrees of Heart Block

First-Degree Heart Block

This obtains when the P-R conduction time in the electrocardiogram is prolonged beyond 0.20 seconds in adults or is longer than it should be for the age of the patient (Fig. 31 *A* and *B*). When prolongation results from digitalis the drug should be discontinued for a few days or the dosage reduced until normal limits of conduction are restored. Specific therapy is not directed toward the abnormality in the P-R time when the defect is a consequence of active rheumatic carditis, diphtheria, or arteriosclerotic heart disease.

Second-Degree (Partial or Incomplete) Heart Block

This is said to be present when some of the impulses from the sinus node are blocked from reaching the ventricles, so that the expected ventricular contractions fail to occur (Fig. 31 *C*). Every second or every second and third stimulus may be blocked and result in 2:1 or 3:1 heart block respectively (Fig. 31 *D, E, F*). On the other hand there may be the *Wenckebach phenomenon*, in which the P-R conduction time gradually and progressively increases until an impulse is blocked and a beat is dropped (Fig. 31 *C*). This defect can be diagnosed clinically with a high degree of accuracy without electrocardiograms in patients who are on a digitalis schedule and in those suffering from active rheumatic carditis, if its occurrence is kept in mind. Ergotamine 30 mg. intravenously in certain instances has been reported to bring out latent heart block in active rheumatic carditis. High-grade block may be a congenital defect.

When incomplete heart block results from digitalis, the drug should be discontinued for a few days or the dosage reduced until the defect is corrected by excretion of the drug. When incomplete heart block occurs, for instance, in active rheumatic carditis or in arteriosclerotic heart disease, digitalis may be given if required because of congestive heart failure without increasing the degree of the block. If the irregularity due to incomplete heart block distresses the patient, atropine 0.0006 Gm. may abolish it.

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damaging auriculoventricular conduction system since patient had myocardial infarction with posterior base configuration of electrocardiogram.

E, another instance of 2:1 heart block. P waves are identified by "P." Blocked P wave is on the upstroke of negative T wave. P-R time, 0.42 second when followed by a QRS complex. Bundle branch block is present, QRS time being 0.14 second. Lesion of conduction system was organic, there was compensatory hypertension.

F shows Lead II of 3:1 heart block. There are three P waves (*PP*) to each QRS complex.

[illegible]

P [illegible]

[illegible] tricular complexes (Lead II). P waves are identified. Auricular rate is 83 per minute. Ventricular rate is 24 per minute. Etiology was congenital heart disease with interventricular septal defect.

I shows auricular fibrillation with complete heart block and idioventricular rhythm (Lead I). Ventricular rate is 36 per minute. Complete heart block was due to digitalis.

Complete Heart Block

Complete heart block or *complete auriculoventricular dissociation* is present when all sinus excitations are blocked from reaching the ventricles. When this occurs the ventricles "escape" and take up their own inherent rhythm. This rhythm known as *idioventricular rhythm* is a response to stimuli arising in the idioventricular center located at the end of the bundle of His just before its bifurcation into right and left bundles. The rate of discharge from this center is usually slow, 30 to 40 per minute, but rarely may be rapid—especially in congenital heart block. Complete heart block may occur with the auricles beating under the direction of the sinus node (Fig. 31 *G* and *H*) or auricular fibrillation may prevail (Fig 31 *I*). Complete heart block is recognized in the electrocardiogram by the occurrence of slow, regular QRS complexes, by auricular complexes which are more rapid, and by a complete dissociation of these two components, since no correlation between them can be detected (Fig. 31 *G* and *H*). The QRS complexes usually have the supraventricular form with normal duration of QRS conduction, but they are of course abnormal in configuration when bundle branch block is present (Fig. 31 *E* and *F*). Occasionally in complete heart block normal conduction of the sinus impulse through the auriculoventricular conduction system to the ventricles occurs.

Although the functional capacity of the heart is compromised by complete heart block, patients manage very well when the rhythm becomes established The stroke volume is greater than that of a normal heart but this expedient alone cannot raise the total cardiac output per minute to normal levels because of the slow rate (Stewart) Spontaneous reduction in basal metabolic rate in patients with complete heart block is an interesting compensatory mechanism to spare the heart.

Complete heart block occurring in the course of rheumatic activity usually disappears spontaneously. It may be a permanent residual of diphtheria. When it occurs in myocardial infarction due to septal involvement, or in syphilitic and in arteriosclerotic heart disease, it indicates underlying myocardial damage or progressive disease

Complete heart block may be congenital. Campbell has recently pointed out that congenital complete heart block is not rare and may be overlooked because the rate is relatively rather fast, between 40 to 56 beats per minute. He is of the opinion that if there are no special complications carrying special risks of their own the prognosis may be good, and that the condition is compatible with survival to old age

Barton and LaDue have pointed out the relative infrequency of women with congenital complete heart block who have become pregnant. They believe that pregnancy should be allowed to continue to term provided associated congenital defects do not constitute an indication for therapeutic abortion.

Complete heart block may be transient or permanent When complete heart block is permanent no specific treatment is required Patients with this defect may lead active and useful lives. They are advised to avoid strenuous exertions as the heart rate is usually unable to accelerate more than a few beats to compensate for exercise. If heart failure occurs digitalis may be used as in other patients requiring it.

When digitalis is the cause of complete heart block, the drug should be discontinued until the block has disappeared In a patient with normal rhythm receiving digitalis it should be suspected when the rate becomes slow and is regular and auricular contractions can be heard on auscultation of the heart without any relationship to the ventricular beats. Its presence should be suspected when digitalis is being given to a patient with auricular fibrillation and the rate becomes slow and the ventricular beats are regularly spaced.

ADAMS-STOKES SYNDROME. The onset of complete heart block may be associated with the symptoms known as Adams-Stokes syndrome—syncope with convulsions, the symptoms may be milder so that there is only faintness and dizziness. With the onset of complete heart block there may be a lapse of several seconds of ventricular asystole before the idioventricular center takes over, and during this time the circulation is at a standstill. The blood pressure falls Cerebral anoxemia results in syncope and muscle twitchings. When the idioventricular center takes over pacemaking, the rate is slow and a short interval is required for circulatory adjustments to be made When this has been achieved the cardiac output, even with the slow rate, is usually adequate to meet the body requirements, the patient recovers from syncope; and convulsions cease The rhythm may later return to normal sinus rhythm or auricular fibrillation and then with each recurrence of complete heart block Adams-Stokes attacks may recur Patients who have permanent complete heart block may suffer attacks of Adams-Stokes syndrome when the rate which has been slow, perhaps around 30 per minute, suddenly slows further to 15 per minute This occurs because of further decrease in volume output of the heart with further decline in the heart rate.

Although the original description of Adams-Stokes attacks apply to syncope and convulsion occurring with complete heart block, attacks which are similar in their clinical manifestations and indistinguishable from them in the cerebral manifestations may be due to ventricular paroxysmal tachycardia, transient ventricular fibrillation, and cardiac asystole due to carotid sinus hypersensitivity or to glossopharyngeal neuralgia. Examination of the heart during an attack may permit the dignosis of ventricular paroxysmal tachycardia or ventricular fibrillation if occasional irregular contractions should be heard. If auscultation should be made only during the period of asystole, complete heart block and asystole due to carotid sinus syndrome could not be differentiated The circumstances under which the attack occurred, analysis of the rhythm following the attack, and the history may aid in diagnosis An electrocardiogram taken during an attack, however, might be required to be certain of the diagnosis In fact, instances have been reported in which syncope in the same patient has been at one time due to ventricular asystole on a background of complete heart block, at other times due to ventricular paroxysmal tachycardia, which resembled ventricular flutter in the printed records, and, on other occasions still, due to ventricular fibrillation All these rhythms were recorded electrocardiographically

Treatment may be considered under the following points:

1. When Adams-Stokes attacks occur frequently, *epinephrine 0 5 to 1 0 cc.* of a 1:1000 solution should be given hypodermically to increase the irritability of the idioventricular pacemaker and of the ventricular muscle in an attempt to increase the rate The drug may prevent long periods of asystole. Its effect, which

lasts from one to two hours, may be prolonged by using epinephrine in oil. The drug should be repeated when attacks recur. On the surface it may appear useless to give epinephrine *during Adams-Stokes attacks when the circulation is slow* or at a standstill. Nevertheless it should be given in order to prevent an immediate recurrence of complete heart block with Adams-Stokes syndrome. If syncope is prolonged, intracardiac injection of epinephrine may be undertaken. In chronic *complete heart block with Adams-Stokes attacks due to periods of further slowing* of the rate, epinephrine may be required for several days until the attacks become less frequent.

2. In certain instances oral doses of *ephedrine sulfate* 20.0 to 30.0 mg. three *times a day may prevent attacks. The effects of this drug* are of longer duration than those following epinephrine.

3. *Barium chloride* 30.0 to 40.0 mg given three or four times a day orally may increase irritability of the heart muscle and prevent attacks

4. *I do not subscribe to the use of thyroid extract* 0.1 *Gm. one to three times* daily in the treatment of complete heart block. It appears inadvisable to increase the basal metabolic rate in patients in the age group in which coronary artery disease occurs Besides, lowered basal metabolic rate is one of the mechanisms by *which the human organism compensates for the slow heart rate.*

5. When the block is of vagal origin, *atropine* 0.5 to 1.0 mg. orally or hypodermically may alleviate it.

6. Fifty cubic centimeters of a 50 per cent solution of glucose has been used *intravenously in the treatment of Adams-Stokes syndrome due to complete heart* block. I have not had occasion to use it.

7. *Digitalis* in full therapeutic amounts may prevent Adams-Stokes attacks I have recently seen it used effectively in two patients in whom attacks had been occurring so frequently that many injections of epinephrine were required in 24 hours

If hypersensitivity of a carotid sinus is the cause of transient complete heart block it should be appropriately treated (Chapter 25).

Wolff-Parkinson-White Syndrome
(Short P-R–Long QRS Syndrome)

The Wolff-Parkinson-White syndrome is usually accepted as a congenital anomaly of the conduction system which is recognized in electrocardiograms by the association of a short P-R time and a prolonged QRS time (Fig. 29 *D*) It is a pre-excitation phenomenon. One explanation of this anomaly is the presence of an accessory pathway of conduction from auricles to ventricles such as might be supplied by the bundle of Kent. The short P-R would be due to the excitation wave arriving at one ventricle by the shorter route and making that ventricle contract early; the prolonged QRS would be accounted for by the summated effect of the asynchronous contraction of the two ventricles, the one contracting early as a result of the stimulus arriving by way of the bundle of Kent, the other ventricle contracting later as a *consequence of the stimulus arriving later by the* excitation wave passing over the usual pathway down the bundle of His

In most instances these time relations remain fixed. Instances are recorded in

which shifts to the normal relationships occur spontaneously, or under such influences as atropine, exercise, quinidine, and digitalis. So far as we know there are no alterations in the functional capacity of the heart. These subjects are prone to attacks of paroxysmal rhythms with a rapid rate arising in the auricles, namely auricular fibrillation, auricular flutter, and auricular paroxysmal tachycardia, or the paroxysms may be due to nodal or to ventricular paroxysmal tachycardia (Fig 29 *C* and *D*) It now appears that this conduction anomaly may be the cause of the refractory character of some cases of these paroxysms. Death has been recorded from the failure of the circulation with persistence of rapid rhythm. In our clinic we have seen attacks of paroxysmal tachycardia persist for many weeks During this time the patient was confined to bed, for the greater part of the time he was in a state of circulatory shock, residence in an oxygen tent was required; at other times still, treatment was required to combat congestive heart failure

Wolff-Parkinson-White syndrome is an electrocardiographic diagnosis but we have come to suspect the presence of this syndrome when a history is secured of prolonged paroxysms of tachycardia which defy the usual therapeutic measures. Patients who have this syndrome even without history of paroxysms should be advised of their possible appearance. This defect has occasionally been associated with other congenital cardiac anomalies, such as patency of the interventricular septum.

Wolff Parkinson-White syndrome requires no treatment per se.

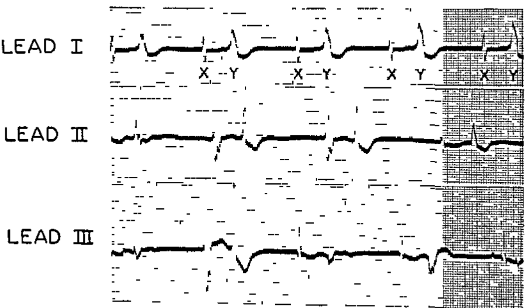
VENTRICULAR RHYTHMS

Idioventricular Rhythm

Idioventricular rhythm occurs in complete heart block and in auricular standstill In the former, stimuli from the sino-auricular node are blocked so that they do not pass down the auriculoventricular conduction system. In the latter, the sinus node fails to send out stimuli, accordingly the ventricles contract in response to stimuli arising in the idioventricular center, which is located just before the bifurcation of the auriculoventricular bundle

The rate of discharge from the idioventricular center is slow, around 30 per minute, and the QRS complexes in the electrocardiogram have the supraventricular form (Fig 31 *G* and *H*) unless bundle branch block is present. The auricles may beat under the influence of the sinus node (Fig 31 G and *H*), auricular fibrillation may be present (Fig 31 *I*), or there may be auricular standstill. Idioventricular rhythm differs from auriculoventricular rhythm in that in the latter rhythm both the auricles and the ventricles beat as a result of stimuli arising in the auriculoventricular tissue

The treatment of idioventricular rhythm when it occurs in association with complete heart block has been described under that section (p. 167). When this rhythm occurs as a manifestation of a hypersensitive carotid sinus it is treated appropriately The management of this rhythm in auricular standstill has been described on page 127



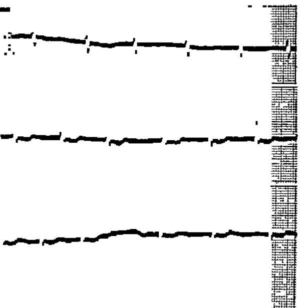


Fig 32

Digitalis Intoxication in a Woman 52 Years of Age Patient exhibited rheumatic heart disease with mitral stenosis and mitral insufficiency Was admitted to the hospital with nausea and vomiting and yellow vision Coupling rhythm was observed on December 16, 1935, but digitalis was continued even though these symptoms of intoxication were present Digitalis discontinued January 18, 1936

Electrocardiogram taken January 20 shows auricular fibrillation with coupled rhythm due to recurrent ventricular premature contractions X indicates normal beat, Y indicates ventricular premature contraction from right ventricle According to pulse deficit chart, coupling stopped January 25. In electrocardiogram taken January 27, auricular fibrillation is present with ventricular rate of approximately 85 per minute. Ventricular premature contractions no longer occur

Ventricular Escape

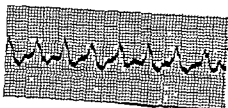
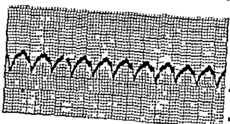
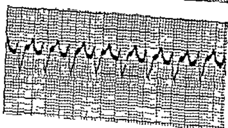
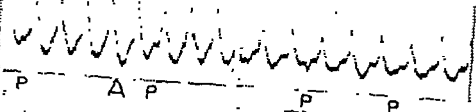
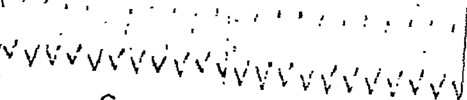
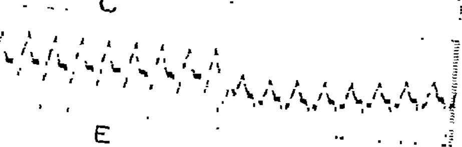
When the rate of discharge from the sino-auricular node is retarded and the activity of the auriculoventricular node is also depressed, and a stimulus is not dispatched to the ventricles, there may be ventricular escape of one or more beats arising from the idioventricular center. It may occur in normal individuals and can be easily provoked in subjects with hypersensitive carotid sinuses (Figs. 57, 58, and 59). In the former it requires no treatment, and in the latter may require appropriate therapy.

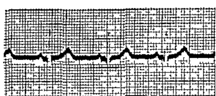
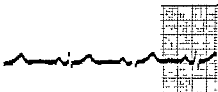
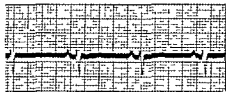
Ventricular Premature Contractions

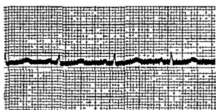
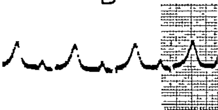
When an abnormal stimulus arises in the right or left ventricle, a premature contraction results. Ventricular premature contractions may occur singly, occasionally, or frequently, and according to a pattern (Fig. 32). On rare occasions the stimulus giving rise to the ventricular premature contractions passes backward through the auriculoventricular conduction system to the auricles. It has been recorded in electrocardiograms and is called *retrograde conduction*. In normal sinus rhythm a ventricular premature contraction is followed by a "compensatory pause." The next stimulus from the sino-auricular node by way of the auriculoventricular conduction system usually finds the ventricles refractory because they have just contracted prematurely, consequently the ventricles do not respond to this excitation The next sinus excitation evokes a normal response. Since the duration of the compensatory pause depends upon the rate of sinus discharge and how early the premature contraction occurs it may not be long enough to be a characteristic feature for distinguishing ventricular premature contractions from auricular ones.

Ventricular premature contractions in the electrocardiogram are characterized by the wide split QRS complexes which are not preceded by P waves, and by T waves which are usually opposite in direction to the main deflection of the QRS complexes Frequently when normal rhythm is present the P wave due to the sinus discharge can be identified either before, in, or after the premature QRS complexes When auricular fibrillation prevails the premature contractions are recognized by their typical configuration (Fig 32) The direction of the major QRS deflection in Lead I, whether up or down, allows localization of the ventricular premature contraction as arising from the right or left ventricle respectively.

Ventricular premature contractions can be induced by mechanical or electrical stimulation of the ventricles They may occur in organic heart disease, as well as in subjects without demonstrable cardiac lesions, and are seen in acute infections as well as in chronic heart disease resulting from arteriosclerosis, hypertension, and rheumatic fever They occur in coronary thrombosis. They may result from overdigitalization when the common pattern may be coupling due to ventricular premature contractions after each normal heart beat (Fig 32) On the other hand, when ventricular premature contractions are associated with heart failure they may disappear on digitalization, followed by regression of the signs and symptoms of heart failure. They may result from nervous tension, loss of sleep, and overindulgence in alcohol and tobacco







LEAD I
LEAD II
LEAD III
1-12-40
2- 1-39
4-14-37
P
A
P
P
P
C
E



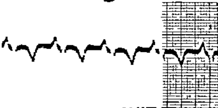
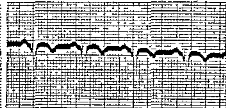



Fig 33

Ventricular Paroxysmal Tachycardia in Patients with Normal Sinus Rhythm, Illustrating the Use of Quinidine in Treatment

A and B relate to a man 63 years of age A, taken January 12, 1940, shows ventricular paroxysmal tachycardia. Rate is 170 per minute Occasional notching can be seen which corresponds to P waves of auricles contracting under stimulus of sinus node QRS complexes are like ventricular premature contractions and are upright in all leads B was taken on October 24, after restoration of normal sinus rhythm at a rate of 68 per minute by use of quinidine Paroxysms in this patient could usually be terminated by quinidine Ration doses of quinidine were usually effective in preventing attacks

C and *D* relate to a man 33 years of age *C*, taken February 1, 1939 shows ventricular paroxysmal tachycardia at 206 per minute *D* was taken February 2, after restoration of normal sinus rhythm by use of quinidine

E and *F* relate to a man 43 years of age *E*, taken April 14, 1937, shows ventricular paroxysmal tachycardia. Rate is 163 per minute QRS complexes are down in all three leads *F* was taken the next day, April 15, after reversion to normal sinus rhythm at a rate of 88 per minute following use of quinidine. Paroxysm occurred in a patient suffering from acute myocardial infarction

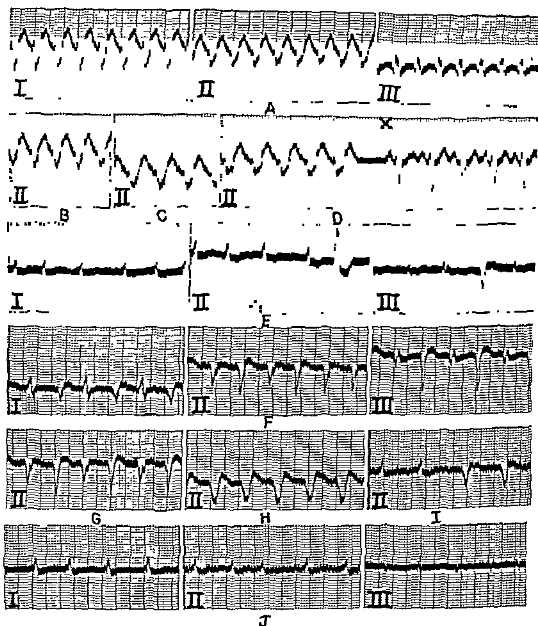


Fig. 34

Effect of Pronestyl in Ventricular Paroxysmal Tachycardia

[illegible] years of age, suffering from acute coronary thrombosis. [illegible] 10, 1950, shows ventricular paroxysmal tachycardia, [illegible] own in B, taken immediately before, and C and D immediately afterward during intravenous injection of pronestyl. In C ventricular rate is slower and QRS time has increased from 0.12 to 0.14 second. D, taken in the eighth minute after injection of 800 mg. of pronestyl, shows the reversion from ventricular paroxysmal tachycardia at a rate of 150 per minute to normal sinus rhythm at X, with normal QRS conduction, the rate being 132 per minute. Normal rhythm persisted. Oral pronestyl continued for a few days. It should be noted that *during injection* ventricular rate became slower and QRS time increased.

E to J inclusive relate to a man 63 years of age

Treatment

If patients have no symptoms and are not aware of the premature contractions, they should not have them called to their attention. They usually require no therapy under these circumstances

If precipitating factors can be identified they should be avoided. When the irregularity is due to digitalis leaf the dose of the drug should be decreased or discontinued depending on the frequency of premature contractions If it is due to digitoxin this drug should be discontinued until the premature contractions have disappeared. In digitalis intoxication it is not uncommon for the ventricular premature contractions to occur in a regular pattern, most frequently giving rise to coupled rhythm (Fig 32) and occasionally to trigeminy or quadrigeminy. It is recalled again, however, that if the premature contractions are a consequence of congestive heart failure they may disappear with digitalization. Under other circumstances digitalis may increase the number of premature beats and predispose to ventricular paroxysmal tachycardia or ventricular fibrillation When seen in acute infections they disappear with improvement and recovery and do not require specific therapy.

When the patient is disturbed by ventricular premature contractions—for instance a patient with arteriosclerotic heart disease—*triple bromide* 1 0 Gm. may be given three times a day The patient should be cautioned about a pustular eruption. If this drug is ineffective, *phenobarbital* may be given a trial If the premature beats are persistent and other measures fail, *quinidine sulfate* 0.2 Gm two or three times a day may abolish them When premature contractions have been abolished by this drug, it may frequently be discontinued without their recurrence. Adequate precaution should be taken to prevent toxicity when quinidine is used over a long time (Fig 22) (see Auricular Fibrillation, p 147). I do not subscribe to the routine use of quinidine sulfate in coronary thrombosis in the presence of ventricular premature contractions with the notion of preventing paroxysmal tachycardia, or as a prophylactic measure before the occurrence of either ventricular premature contractions or ventricular paroxysmal tachycardia Papaverine and potassium salts are occasionally used as for auricular premature contractions (p 134) The use of procaine amide hydrochloride is mentioned on page 178

Ventricular premature contractions do not require therapy in most of the situa-

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E, taken on October 10, 1950, shows auricular fibrillation (ventricular rate 120 per minute) with one premature ventricular contraction in Leads II and III Because ventricular rate did not retard adequately on admission to hospital on February 22, 1951, digitalis was given for several days both orally and intravenously Ventricular paroxysmal tachycardia resulted as shown in F (three leads) taken on February 27, 1951 Ventricular rate was 158 per minute and there was alternation of complexes from one ventricle to the other, usually a grave finding He was given pronestyl intravenously G, taken immediately before, shows alternation of focus between the two ventricles The QRS time was 0 12 second H, taken during injection of pronestyl, shows that

after 600 mg of pronestyl intravenously in a 6 minute period Auricular fibrillation persisted Oral pronestyl continued for a few days

tions in which they are encountered. On the other hand, they may be the forerunners of ventricular paroxysmal tachycardia or ventricular fibrillation. Their frequency and the circumstances under which they occur are important in the choice of therapy.

Ventricular Paroxysmal Tachycardia

Ventricular paroxysmal tachycardia is a rhythm, usually rapid, which results from stimuli arising from an irritable focus in one of the ventricles and is characterized by sudden onset and sudden disappearance. The rhythm is not so accurately regular as is auricular paroxysmal tachycardia (Fig 33). Occasionally the site of origin may alternate between the two ventricles (Fig. 34 F and G) The rhythm may be looked upon as a series of ventricular premature contractions. The mechanism may depend upon the maintenance of a circus motion in the ventricles. When the preceding cardiac mechanism is normal sinus rhythm the auricles continue to beat under the guidance of the sinus node. Loosening the galvanometer string so that 1 millivolt gives a 2-cm. deflection instead of 1 cm. may show the presence of P waves When auricular fibrillation precedes this rhythm, the auricles continue to fibrillate (Fig. 34). The ventricular rate is rapid, commonly between 150 and 200 beats per minute.

The rhythm may occur for a few beats or last for days, and may be resistant to treatment, especially in patients with Wolff-Parkinson-White syndrome The circumstances under which this rhythm usually occurs require its termination as soon as possible. It is an ineffective rhythm, and is associated with decreased cardiac output per minute and per beat, rise in venous pressure, and prolongation of circulation time. It is rarely seen in normal individuals. It occurs more frequently in older than in younger persons, and especially in the presence of hypertensive and arteriosclerotic heart disease.

The prognosis is more serious in the older age groups. Immediate therapy is imperative when it occurs as a complication in myocardial infarction. If this rhythm persists, and the blood pressure falls and the coronary blood flow is decreased with the lowered cardiac output, myocardial infarction without coronary thrombosis may occur The T waves and the RS-T segmental changes which indicate myocardial damage should not be regarded simply as alterations associated with the paroxysmal tachycardia, but proper significance should be attached to the pathologic process in the heart muscle Patients should be treated appropriately and adequate time allowed for healing of the infarct to take place

Treatment

Patients should remain at rest in bed The main problem is to stop the attack and later to direct measures toward the prevention of recurrences

When this rhythm occurs in digitalis intoxication the drug should be discontinued. Use of quinidine under these circumstances may result in alternation of the ventricles, which is usually fatal, or may cause ventricular flutter or ventricular fibrillation. Under these circumstances *pronestyl* should be used intravenously (p. 178 and Fig 34). When the rhythm occurs in patients with Wolff-Parkinson-White syndrome it may not respond to any measures which have been available, with the possible exception of pronestyl. Carotid sinus pressure usually has no effect.

QUINIDINE. Quinidine has been the drug of choice in the treatment of ventricular paroxysmal tachycardia. In certain instances, however, pronestyl appears to be more appropriate to use. In most instances quinidine is effective in terminating this rhythm. It appears that *synthetic quinidine sulfate* may be substituted for quinidine derived from the cinchona bark. The required dosage is very variable. The rhythm usually occurs under circumstances that do not warrant the delay which would be necessary to test for sensitivity to quinidine (p. 148). Accordingly 0.4 Gm. of the drug may be given at once and repeated every four hours. A total of 3.0 to 4.0 Gm. may be required in 24 hours before reversion to normal rhythm or to auricular fibrillation occurs. If the patient's condition is satisfactory and there is no great urgency, 2.0 Gm. may be given the first 24 hours, and 3.0 Gm. the second 24 hours. Auscultation of the heart should be carried out frequently in order to detect increase in its rate or in irregularity that may be the forerunner of ventricular fibrillation. Electrocardiograms should be taken when possible. While the drug is being given the ventricular rate usually declines and reversion to normal rhythm (Fig. 33) or to auricular fibrillation ensues. Following this reversion 0.2 Gm. may be given two or three times a day for two to three days. Amounts larger than those given may be required if the rhythm persists, which may be the case in Wolff-Parkinson-White syndrome. The larger amounts are used with increased caution.

Rarely it may be necessary to use *quinidine hydrochloride* 0.2 to 0.3 Gm. intravenously. *Quinidine lactate* is soluble and may be given intravenously in 0.3 to 1.2 Gm. amounts. The smaller dose should be used in the first attempts. Reversion to normal rhythm or auricular fibrillation occurs within a few minutes. An adequate interval should be allowed before subsequent doses are given, if reversion does not occur on the first attempt, in order not to induce toxic effects from accumulation. After reversion has occurred quinidine sulfate is given in the usual amounts when maintenance appears indicated. Emphasis is again placed on the caution with which quinidine should be used intravenously and on the fact that its administration by this route is rarely required. The introduction of procaine amide hydrochloride supplies the need for a rapidly acting intravenous drug. Variability of absorption from the gastrointestinal tract when quinidine is given orally may be circumvented by using the drug intramuscularly. A soluble quinidine preparation for intramuscular injection has these ingredients: quinidine hydrochloride 15 Gm., antipyrine 15 Gm., urea 20 Gm., and distilled water to 100 cc. Of this solution 3.75 to 5.0 cc. (quinidine 0.45 to 0.6 Gm.) may be used as the initial dose. Its effect of slowing the heart rate, which may be apparent in 15 to 30 minutes, is maximal in one and a half to three hours. Subsequent smaller doses are given at two hour intervals if reversion to normal rhythm has not resulted from the initial dose. Maintenance amounts of 0.2 to 0.6 Gm. of this preparation every four to eight hours may be given for two to three days after this rhythm has been terminated, if quinidine cannot be administered orally.

Quinidine 0.2 Gm. two or three times a day may be effective in preventing attacks of recurrent ventricular paroxysmal tachycardia. When it is given over long periods of time the appearance of ventricular premature contractions as well as prolongation of QRS conduction time should be detected in electrocardiograms.

DIGITALIS. Digitalis is usually *contraindicated* in the presence of ventricular paroxysmal tachycardia because it may lead to ventricular fibrillation or to alterna-

tion in the direction of the QRS complexes. Occasionally ventricular paroxysmal *tachycardia cannot be abolished* and heart failure appears; in such cases there may be no alternative but to use digitalis.

Ventricular paroxysmal tachycardia with alternation of the two ventricles may *result either from digitalis* (*Fig.* 34 *F* and *G*) or from quinidine, or from the simultaneous use of the two drugs (Fig. 19). If it is due to one or the other of the two drugs alone the offending drug should be discontinued. When it occurs while *both drugs* are being used they are both discontinued. Ventricular paroxysmal tachycardia with alternation is usually fatal. It may be the precursor of ventricular fibrillation. The use of magnesium sulfate intravenously may be tried in this bi-*directional* type of ventricular paroxysmal tachycardia. Procaine amide hydrochloride has been successfully used intravenously in such cases.

PROCAINE AMIDE HYDROCHLORIDE. Pronestyl hydrochloride* (procaine amide hydrochloride) has recently been used in the treatment of paroxysmal tachycardias It has been found effective in terminating attacks of ventricular and auriculoventricular paroxysmal tachycardias but its effectiveness in the other types has not been established so precisely.

In the treatment of ventricular and auriculoventricular paroxysmal tachycardia if there is urgency 200 to 1000 mg. (not more) may be given intravenously slowly, not more rapidly than 200 mg. per minute. *It is safer to inject from* 50 to 100 mg. per minute. Normal rhythm is restored after 200 mg. or more. Intravenous injection of the drug induces hypotension. The blood pressure should therefore be taken *during injection at frequent intervals, and the injection slowed up or discontinued* if the blood pressure sinks too rapidly and too far. Continuous auscultation of the heart and a continuous electrocardiogram are also recommended during injection. *Injection is discontinued with the restoration of normal rhythm. Oral doses* in 0.5-Gm. amounts every four to six hours may be used for a few days afterward as a prophylactic measure During intravenous injection of the drug in the presence of *ventricular paroxysmal tachycardia, the rate slows and the QRS complexes widen* (Fig. 34) with moderate prolongation of the QRS time. It has restored normal rhythm promptly in 12 attacks in 7 patients It was effective in terminating 11 paroxysms of nodal tachycardia in 8 patients to whom it was given intravenously. It has also been effective in terminating attacks of ventricular paroxysmal tachycardia due to digitalis intoxication (Fig. 34 *F-J*).

The drug may be used orally to restore normal rhythm in these two rhythms. This is probably the safer route. A first dose of 1.0 Gm followed by 0.25 to 0.5 Gm. at four- to six-hour intervals is usually adequate, but larger doses at shorter intervals may be required. Hypotension and electrocardiographic changes do not occur when it is given orally. Restoration of normal rhythm may occur one-half to several hours after the initial dose. In our experience it has been effective orally in 2 patients with ventricular paroxysmal tachycardia and in 3 patients with auriculoventricular paroxysmal tachycardia

Pronestyl is also effective in the treatment of ventricular premature contractions and is useful when they result from digitalis. It is effective orally in 0.25- to 0.5-Gm. amounts every four to six hours. *It is said to be useful intravenously in 100- to*

* E R. Squibb and Sons.

500-mg amounts in the treatment of ventricular rhythms occurring during anesthesia. Hypotension does not occur in anesthetized patients.

Urticaria may result when the drug is given orally over long periods of time. Pyribenzamine may be given if it appears necessary to continue to use the drug One instance of agranulocytosis has been recorded.

Since the drug can be given intravenously and is effective within a matter of minutes it has the advantage over quinidine, which I do not think should be used by this route Pronestyl has been effective in the instances we have used it in the treatment of ventricular and nodal paroxysmal tachycardia I have had occasion to use it once effectively in 2 1 auricular paroxysmal tachycardia due to digitalis and once in auricular flutter, and other investigators have reported that it is occasionally effective also in auricular fibrillation. I have seen no untoward results In the treatment of cardiac arrhythmias the full role of this drug, which appears to have a specific action on depressing the ventricular muscle and the specialized auriculoventricular tissue, remains to be delineated

MAGNESIUM SULFATE. The intravenous injection of 20.0 cc. of a 20 per cent solution of magnesium sulfate may be effective in terminating an attack of ventricular paroxysmal tachycardia. As we have already mentioned, it might be tried in cases of bidirectional ventricular paroxysmal tachycardia due to digitalis, to quinidine, or to digitalis and quinidine should pronestyl not be available It should not be used if the patient has had bundle branch block or complete heart block before the onset of the paroxysm

ATROPINE. In animals the intravenous injection of atropine prevents the ventricular paroxysmal tachycardias which usually follow rapid intravenous injection of epinephrine. This effect has been attributed to increasing the rate of discharge from the ventricular focus. As a consequence the sinus node takes over pacemaking

It has therefore been suggested that atropine might be used in myocardial infarction to prevent the occurrence of ventricular paroxysmal tachycardia In my opinion, however, this plan of therapy should not be followed Atropine increases the heart rate and thereby increases the work of the heart—two effects which should not be induced in the presence of myocardial infarction

Ventricular Fibrillation

In ventricular fibrillation coordinated contraction of the ventricles is abolished and is replaced by rapid irregular twitches of the ventricular muscle. Its persistence is incompatible with life since these twitchings are ineffectual in expelling blood from the ventricular cavities However, brief paroxysms have been recorded which were not fatal They may result in attacks of syncope which simulate Adams-Stokes syndrome in complete heart block This rhythm is associated with fall in blood pressure to zero, and absence of pulse and of heart sounds With restoration of coordinated activity of the ventricles the symptoms disappear and patients recover spontaneously. Ventricular fibrillation may be the terminal cardiac mechanism in patients dying from any cause It is more common in patients with arteriosclerotic heart disease. It may follow massive doses of quinidine and digitalis *simultaneously* or of either of the drugs alone

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The diagnosis of ventricular fibrillation can only be made electrocardiographically.

The QRS complexes are wide and split, and of varying form and amplitude, and they occur at irregular intervals There is no coordinated activity of the heart. There may be a history of occurrence of the attacks of syncope at intervals, the patient may be fortunate enough to be seen by a physician or be in a hospital and have an electrocardiographic record made during an attack.

Treatment

If the episodes of ventricular fibrillation are not due to quinidine or digitalis and the patient is not receiving either of these drugs, quinidine may be used. Quinidine probably cannot be given intravenously in time to be effective for any one attack of syncope. It may, however, prevent recurrences It may be given by mouth in ration doses if the attacks are frequent enough for its effectiveness to be gauged. Ration doses are not usually advocated for patients with complete heart block or bundle branch block. Its use might be required if attacks of ventricular fibrillation occur with great frequency.

Digitalis should not be used when ventricular fibrillation is suspected

On the basis of animal experiments Lindner and Katz have suggested the use of papaverine hydrochloride as a preventive for ventricular fibrillation when it is anticipated. Its intravenous use may not be without danger.

When attacks are recurring frequently and are leading to repeated episodes of syncope, procaine hydrochloride may be given intravenously as 0.1 per cent solution; around 300 cc may be given. The use of procaine for this purpose is new and has not been fully explored. It has found use recently in the treatment of cardiac arrhythmias, in cardiac arrest, and in ventricular fibrillation occurring during surgical anesthesia. Procaine amide hydrochloride may be effective in the treatment of ventricular fibrillation (p 178).

Ventricular Fibrillation and Cardiac Arrest During Surgical Anesthesia

Ventricular fibrillation and cardiac arrest are more likely to occur during the use of cyclopropane, chloroform, and nitrous-oxide–ether than with ether and oxygen. Giving epinephrine to experimental animals during chloroform anesthesia causes ventricular fibrillation This drug enhances the rhythmicity of the ventricular foci The spontaneous occurrence of ventricular rhythm during clinical anesthesia may be due to the effect of these anesthetics in increasing the sensitivity of the heart muscle to epinephrine The increased sensitivity may be due to the concentration already in the blood or to increased amounts which may be elaborated under excitement. Moreover anoxia may increase the sensitivity of the heart to epinephrine.

During anesthesia there may be cardiac arrest owing to cessation of activity of the sinus node (known as cardiac standstill) or there may be cessation of cardiac function owing to ventricular fibrillation In cardiac standstill ventricular fibrillation is one of the rhythms which the heart exhibits with the return of cardiac activity. When cardiac arrest occurs at operation the heart should be exposed quickly and massaged at regular intervals at a rate of about 40 per minute; procaine hydrochloride or procaine amide hydrochloride should be administered.

Burstein suggests the use of procaine infusion in order to prevent the occurrence of these rhythms. Up to 300 cc. of a 0.1 per cent solution may be given one hour

before operation One gram of procaine is dissolved in one liter of normal saline. If arrhythmia develops during anesthesia 100 0 mg. procaine (10 cc. of a 10 per cent solution) is given intravenously rapidly. This concentration of the drug can be given only when the patient is under general anesthesia, because effects of the drug on the central nervous system result unless the patient is anesthetized.

Ruzicka and Nicholson recommend the following regimen for cardiac arrest under anesthesia: (1) artificial respiration with 100 per cent oxygen through an endotracheal tube; (2) cardiac massage through the diaphragm or through the thorax, whichever will allow the most rapid approach to the heart, depending on the operation being done at the time; and (3) combined use of procaine and epinephrine at once while (1) and (2) are being prepared. One hundred milligrams (10 cc of a 1 per cent solution) of procaine hydrochloride are given first intravenously or by intracardiac injection This is followed by the injection of 0 5 cc. of a 1:1000 solution of epinephrine in 9 5 cc. of isotonic sodium chloride solution into the left ventricular cavity *The two drugs may be combined so that 0 5 cc. of* 1:1000 epinephrine in 9 5 cc. of a 1 per cent solution of procaine hydrochloride are given intravenously or into the left ventricular cavity.

These authors point out that epinephrine causes arrhythmias and ventricular fibrillation in sensitized hearts and that final experience may indicate that procaine plus massage may be as beneficial as or even more effective than the combination with epinephrine. If cardiac activity has not been restored by the time the heart is exposed, repetition of the procaine and epinephrine injection is indicated

Beck and his associates recommend the following regimen for the treatment of ventricular fibrillation occurring during anesthesia· (1) mechanical respiration, (2) the injection of 5 cc. of a 2 per cent solution of procaine hydrochloride into the right heart; (3) active cardiac massage to distribute the drug to the heart muscle, and (4) electric shocks applied to the heart. The heart is placed between two large electrodes and a 100-volt alternating current with an amperage of 1 5 is passed through the heart Several shocks are required to accomplish defibrillation When these procedures are effective the ventricles stop fibrillating, there is a short period of standstill, after which a supraventricular rhythm takes over Massage is continued until cardiac contractions are able to empty the cardiac cavities. Epinephrine or neosynephrine has been used when defibrillation did not follow early shocks

There has been a recent report by Lampson, Schaeffer, and Lincoln of cardiac arrest following the use of cyclopropane in anesthesia during repair of a foot injury The cardiac arrest due to ventricular fibrillation was of 27 minutes' duration Complete recovery ensued Treatment was as follows· Within two to three minutes decision was made to open the chest through the left fifth interspace This was accomplished in ten seconds Ventricular fibrillation could be seen. Cardiac massage was instituted With the index and middle fingers behind the heart, intermittent compression against the sternum was used to keep blood in circulation. Artificial respiration with the anesthesia machine supplied 100 per cent oxygen The color of the patient improved with cardiac massage but normal rhythm did not ensue Fifteen minutes later 3 0 cc of a 1 per cent solution of procaine hydrochloride was given intravenously. A blood transfusion was started 14 minutes after the first injection of procaine. Twenty-six and a half minutes after the onset of cardiac arrest

a second dose of 2.0 cc. of a 1 per cent solution of procaine hydrochloride was given. Thirty seconds later the tone of the heart changed. It stiffened between the massaging fingers and again assumed normal contractions, irregular at first, then becoming regular. Two minutes later the pulse was regular and strong. After one-half hour of observation the chest was closed. Spontaneous respirations started 15 minutes after cardiac arrest and while the heart was still being massaged. Electrocardiographic records showed the presence of ventricular fibrillation and recorded the evolution of the restoration of normal rhythm.

From this experience the authors recommended the *following regimens:*

1 When ventricular fibrillation occurs 5.0 to 10.0 cc. of 1 per cent solution of *procaine hydrochloride* should be given intravenously or directly into the heart. If the fibrillatory movements do not give way to effective coordinate ventricular *contractions, the injection of procaine should be repeated or electric stimulation* applied to the heart.

2. When cardiac standstill is evident, epinephrine, 1.0 cc. of 1:1000 solution, may be injected into the heart cavity or into the heart muscle. If too large an amount is given, the heart in standstill may go into fibrillation. Epinephrine should not be used in ventricular fibrillation as it increases the irritability and makes defibrillation more difficult.

These instances of the treatment of cardiac emergencies associated with anesthesia are cited in detail because the experiences with recovery from cardiac standstill and ventricular fibrillation are few and the proper use of procaine hydrochloride and epinephrine has not yet been clearly enough defined to permit formulation of a definite regimen. Procaine amide hydrochloride may find usefulness in paroxysmal rhythms during anesthesia (p. 178).

Ventricular Flutter

Electrocardiograms have been recorded of patients with ventricular rhythms in which the configuration of the QRS complexes is somewhat similar to that seen in ventricular paroxysmal tachycardia. The rate, however, is more rapid than is commonly seen, and the electrocardiograms look like photographs of the vibrations of a tuning fork This rhythm is sometimes called ventricular flutter. Attempts have been made to explain the mechanism of the rhythm by the concept of the circus motion Ventricular flutter is closely allied to ventricular fibrillation, because, in the same record, the QRS complexes may become irregular and change in amplitude.

Treatment

When this rhythm has been detected the patient should be kept at complete rest in bed Although quinidine is usually the drug of first choice to use in treating this rhythm, I have seen repeated attacks in a patient with Wolff-Parkinson-White syndrome resist all forms of medication. Quinidine given in large amounts was ineffective in this patient and methacholine chloride was used without any hope of its being of benefit. Digitalis, although contraindicated, had to be used because of the onset of heart failure; it did not in this instance increase the gravity of the situation nor did it terminate the rhythm

I have seen with Deitrick and Smith the electrocardiographic records of a patient with complete heart block who had attacks of syncope Some of these attacks were of the Adams-Stokes variety due to ventricular asystole Other attacks of syncope were associated with a ventricular rhythm during which the electrocardiograms had the configuration we are describing as ventricular flutter. Epinephrine was indicated for the Adams-Stokes attacks but was of course contraindicated in the rapid ventricular rhythm because of its tendency to induce ventricular fibrillation. This patient experienced attacks of ventricular flutter when digitalis was discontinued. It was our impression that digitalis increased the cardiac output and consequently the coronary circulation, and that it maintained an adequate oxygen supply to meet the myocardial requirements. With cessation of the use of digitalis and its excretion, the cardiac output decreased, myocardial anoxemia occurred, and ventricular paroxysmal tachycardia or flutter resulted. The report of a case similar to this is in the literature

Procaine amide hydrochloride intravenously or into the cardiac chambers might find application in the treatment of this rhythm (p 178)

PULSUS ALTERNANS

In pulsus alternans the volume of the pulse alternates regularly between large and small It must not be confused with coupled rhythm, in which the grouping of the heart beats is in pairs followed by a pause, although the volume may also alternate (Fig 32). Pulsus alternans may be detected in certain patients on palpation of the radial pulse but can be more easily diagnosed while taking the blood pressure It may be accompanied by a similar rhythm in the electrocardiogram Pulsus alternans is evidence of grave myocardial disease. It is seen in syphilitic heart disease, in arteriosclerotic and hypertensive heart disease, in heart-failure, in coronary occlusion, and in uremia. It requires no treatment per se, but the underlying condition should be accorded appropriate therapy It may occur in paroxysmal tachycardia and auricular flutter as may also electrical alternans

COUPLED RHYTHM

Coupled rhythm is said to be present when the heart beats are grouped in pairs. It may result from a number of causes. The underlying cardiac mechanism should be known before treatment is undertaken. Electrocardiograms are required in many instances for accurate diagnosis. Coupled rhythm may arise in the following ways:

1 It is most commonly due to premature contractions—most frequently ventricular ones—occurring after each usual or normal beat of the heart (Fig 32) Coupling due to ventricular premature contractions in patients with normal rhythm or auricular fibrillation who are being given digitalis usually indicates overdigitalization

2 It may be due to regularly recurring auricular or auriculoventricular premature contractions occurring after each normal beat.

3 It may be due to a blocked auricular premature contraction occurring after every second normal beat.

4. It may be due to 3.2 heart block with the Wenckebach phenomenon, in digitalis intoxication (Fig. 31 C), in active rheumatic carditis, and in arteriosclerotic heart disease.

5. It may be due to sino-auricular block occurring every third expected beat, and may result from digitalis.

6. It may be due to recurrent variation of change in block in auricular flutter.

The following instances of coupled rhythm, however, can frequently be diagnosed clinically without electrocardiograms:

1. *When a patient with auricular fibrillation is being given digitalis and coupling* occurs it is usually due to ventricular premature contractions and usually indicates digitalis intoxication.

2. If a patient with normal rhythm is being given digitalis, and coupled rhythm appears it may be due either *to ventricular premature contractions or to incomplete* heart block, namely 3:2 block with Wenckebach phenomenon.

3. When a patient with active rheumatic carditis has coupled rhythm, it may be due to any variety of the premature contractions but on the other hand may be due to 3:2 heart block with Wenckebach phenomenon.

TRIGEMINAL RHYTHM

Trigeminal rhythm is said to be present when the heart beats fall into groups of threes followed by a pause. It may arise in the following ways.

1. When premature contractions occur after every second beat, the long pause afterward makes the two normal beats and the premature contractions fall together in a group of three. Premature contractions may arise from the auricles, *the ventricles, or the auriculoventricular conduction system.*

2 Trigeminy may result from regularly recurring incomplete heart block, every fourth P wave being blocked.

3. It may be due to interpolated premature contractions, that is, contractions which fall between two normal beats without disturbing the rhythm. They are true extrasystoles *This is the only occasion when it is proper to use the term "extrasystole."*

Interpolated premature contractions may arise from auricles, auriculoventricular tissue, and ventricles If the stimulus occurs near the middle of the R-R interval and the ventricles are no longer refractory, they will respond and recovery will again have taken place by the time the next normal sinus stimulus arrives at the ventricles Trigeminal rhythm has significance only in relation to the mechanism which results in this grouping and the reason for its occurrence. Appropriate treatment should be instituted in each case.

Quadrigeminy is said to be present when the heart beats or pulse occur in groups of four followed by a pause.

BUNDLE BRANCH BLOCK

Bundle branch block, or "intraventricular block," occurs when there is interference with the spread of the excitation wave down one of the branches of the auriculoventricular bundles or both, and through the ventricular muscle mass. This

abnormality is recorded in electrocardiograms. The QRS conduction time is longer than 0 10 seconds which is considered to be the upper limit of normal. The QRS complexes are wide and split.

Multiple precordial leads aid in the localization of the lesion in bundle branch block more precisely than do the three standard leads In such derivations in left bundle branch block the intrinsic deflection in relation to the onset of the QRS is normal in the derivations over the right ventricle, and markedly delayed in those over the left ventricle The opposite is the case in right bundle branch block In left bundle branch block in V_1 there is a small R and deep S or deep QS deflection, with normal intrinsic deflection, elevation of the RS-T segments, and upright T waves. In V_6 there is no Q wave The R wave is tall and split There is a late intrinsic deflection. The RS-T segment is displaced downward and the T waves are negative The ventricular complexes in the limb leads depend on the position of the heart which can be determined from the unipolar limb derivations. In right bundle branch block in V_1 there is a small R, small S, and tall R_1, with late intrinsic deflection and inverted T waves. In V_6 there is a small Q, late R, late wide S waves, normal intrinsic deflection, and upright T waves. The ventricular deflections in the standard limb leads will depend on the position of the heart which can be determined from the unipolar limb leads

Bundle branch block may be a permanent defect or may be transient It may be present for varying lengths of time over days or weeks only to disappear or it may be of more transient occurrence still, so that its onset may be detected while the electrocardiogram is being recorded. It may occur transiently during exercise

The rhythm of the heart is not disturbed by bundle branch block *Exact clinical* recognition is difficult although the asynchronous contraction of the two ventricles may produce reduplication of the heart sounds and a bifid apex thrust.

Bundle branch block induces no symptoms per se but is usually an expression of severe myocardial damage It is found commonly in heart disease due to arteriosclerosis and hypertension, and may follow myocardial infarction It occurs in active rheumatic carditis, in chronic rheumatic heart disease, and in congenital heart disease, especially when a septal defect is present. It may be a functional manifestation in uremia, and may be due to anoxemia in paroxysmal tachycardia It may be transient in pulmonary infarction. Bundle branch block is found in myocarditis of obscure origin with cardiac enlargement, embolic phenomenon, and heart failure, a complex sometimes known as "Fiedler's isolated myocarditis."

Quinidine may prolong QRS conduction time (Fig 22) On rare occasions digitalis has been implicated Widening of the QRS complexes in the Wolff-Parkinson-White syndrome is thought to be the consequence of a congenital variation in the conduction tissue of the heart

Patients with the S wave type of bundle branch block are said to have a normal life expectancy if a year has elapsed after its discovery. When this is the only abnormality the patient can lead a normal life. Patients with other types of bundle branch block need not change their regimen if they have a good functional capacity and are without symptoms Periodic examinations should be made to be aware of progressive damage Special care should be observed when operations requiring anesthetics are necessary. Oxygen should be used to avoid anoxia and care should be exercised not to overload the circulation with fluid.

There is no specific treatment for bundle branch block; the underlying condition is treated if necessary. Its appearance in myocardial infarction implies septal involvement, which may be transient or may remain as a permanent defect. As a manifestation of rheumatic carditis it usually subsides with cessation of rheumatic activity. It may be transient in heart failure, disappearing with recovery from that condition. The use of hypertonic glucose intravenously has caused its disappearance in uremia.

TREATMENT OF ABNORMAL RHYTHMS WHEN EXACT DIAGNOSIS IS NOT KNOWN

Premature Contractions

Ventricular premature contractions can frequently but not always be distinguished clinically from auricular or auriculoventricular premature contractions. If they can be diagnosed and the electrocardiagram is not available for confirmation and the patient is disturbed by them, the appropriate treatment is instituted. Sedatives such as triple bromide and phenobarbital may be effective whatever the type of contraction. Digitalis should not be used because it may increase the number of premature contractions if they are ventricular. In those instances in which the premature contractions of unknown origin do not respond to sedatives, quinidine may be used more safely. Digitalis may eradicate premature contractions which are ventricular in origin if they are associated with heart failure

Paroxysmal Tachycardia

When the origin of paroxysmal tachycardia cannot be localized exactly by clinical examination and electrocardiographic diagnosis is not available, the following measures may be used in turn without any deleterious effect on the specific rhythms deep breathing, holding the breath, and attempts to induce vomiting. Carotid sinus pressure during quiet breathing or deep inspiration may be effective If these procedures are ineffective and termination of the rhythm as quickly as possible is indicated, quinidine should be used. It is recalled that this drug is most effective in ventricular paroxysmal tachycardias but may be effective in the supraventricular type On the other hand, digitalis should not be given in paroxysmal tachycardia of unknown type because the rhythm might be ventricular in origin.

SURGICAL TREATMENT OF PAROXYSMAL TACHYCARDIAS

There have been several reports in the literature in the last twenty years of the treatment of obstinate paroxysms of tachycardia by interruption of the accelerator fibers of the heart, especially on the right side. Leriche and Fontaine reported the successful termination of supraventricular paroxysmal tachycardia in two patients by *bilateral stellate ganglionectomy* In 1938 Coleman and Bennett reported the termination of a prolonged attack of auricular paroxysmal tachycardia by *alcohol injection* of the right stellate ganglion; the patient remained free of attacks four and one half months after operation, whereas frequent attacks had recurred in the twenty years before. In 1939 Leibovici reported the immediate cessation of a pro-

longed paroxysmal tachycardia by *novocainization* of the left stellate ganglion in a 29-year-old patient, ocular pressure, carotid sinus pressure, ouabain, and quinidine had been ineffective in terminating the attack. Mandl in 1925 had also reported the cessation of paroxysmal tachycardia in a patient with angina pectoris, by novocainization of the left stellate ganglion. J C White quotes the successful termination of a prolonged attack of auricular paroxysmal tachycardia in a 4-year-old patient of P. D White and H. L. Higgins after novocainization of the upper right thoracic ganglia four days after novocainization of the left one had been ineffectual Twelve days later, when paroxysmal tachycardia recurred, paravertebral infiltration of the ganglia from T_1 to T_4 with alcohol under general anesthesia terminated the attack and normal rhythm prevailed for three weeks. On recurrence procainization again ended the paroxysm. He also reports another case of P. D White, who experienced complete relief from both paroxysmal auricular fibrillation and angina pectoris after bilateral paravertebral alcohol injection carried out at 12-day intervals The patient experienced relief a second time for one month after repetition of the alcohol injections when auricular fibrillation recurred one and three-quarter years later.

For prolonged attacks of auricular paroxysmal tachycardia as well as of paroxysmal auricular fibrillation with or without angina which do not respond to treatment, White recommends the *interruption of the cardiac accelerator nerves* by the novocainization of the upper thoracic ganglia on first one side, then the other if necessary, in an attempt to restore normal rhythm. In this way it can be ascertained whether the interruption of one or both chains is necessary.

If novocainization is effective, yet the paroxysmal tachycardia recurs, surgical removal of the inferior cervical and upper thoracic sympathetic ganglia can be carried out in patients who are well enough to stand the procedure, and alcohol injection in those individuals with severe coronary artery disease. Ray, however, is of the opinion that in instances of stubborn paroxysmal tachycardia surgical sympathectomy of the inferior cervical ganglion and $T_{1,2,3,\text{ and }4}$ on one side, then on the other side if necessary, is the procedure of choice, rather than preliminary alcohol block This operation would therefore include the stellate ganglion, to which some investigators have wished to confine the novocainization. Surgical sympathectomy can be done under ether and oxygen anesthesia It can be done satisfactorily under local anesthesia provided the pleura is not accidently entered This accident might be serious if expansion of the lungs could not be achieved promptly, a procedure which is possible when intratracheal ether is used as the anesthetic.

SUMMARY

The recognition and treatment of cardiac irregularities has gone a long way since Sir James Mackenzie described auricular fibrillation from polygraphic tracings, and Rothberger and Winterberg, and Lewis independently identified this rhythm in electrocardiographic tracings in 1906, and since the introduction of the string galvanometer by Einthoven in 1903. These were indeed auspicious occasions. As a result of the impetus from these discoveries, the treatment of irregularities

dominated clinical cardiology for some years. Especially was this the case with respect to the use of digitalis, which, for example, was based on the presence of auricular fibrillation because dramatic slowing of the heart rate had been demonstrated in this rhythm after exhibition of the drug. Since then the mechanism of such rhythms as auricular fibrillation and auricular flutter has been explained as a result of a circus motion of the excitation process. It is recalled that Prinzmetal has recently questioned the accuracy of this notion. As time has gone on, accurate clinical and electrocardiographic recognition of the rhythms of the heart has been achieved. In most instances these rhythms can be adequately controlled by drugs which have been available, by new drugs which are being introduced, or by finding new applications for old drugs. Nevertheless there are rare occasions when drugs are ineffective for adequate control of abnormal rhythms. In certain of these surgical interruption of the accelerator mechanism of the heart has brought an end to prolonged, intractable paroxysms of tachycardia. This opens up a new approach to the treatment of these cardiac rhythms. With all the changing emphasis occasioned by developments of new drugs and by the changes in the relative importance of different diseases promoted by these drugs, it must not be forgotten that patients exhibiting cardiac irregularities may be very ill, and that prompt treatment may be life saving The clinical recognition and treatment of cardiac irregularities can still supply some of the most dramatic and satisfying moments that physicians experience

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CHAPTER 6

Congenital Heart Disease

INTRODUCTION

One can afford an attitude of optimism regarding treatment of congenital heart disease Surgical means have been devised for correcting certain of the congenital defects or for converting these into defects having less severe physiologic consequences for the circulation. Furthermore, medical therapy has been provided for one of its most devastating complications, subacute bacterial endocarditis

Means are not available at present for preventing congenital malformations of the heart, since exact data on the factors which give rise to them have not been determined. Recently it has been suggested that maternal rubella during pregnancy may cause congenital malformations of the newborn. However, this infection will have to be traced in a large number of pregnant mothers, and its effect on the offspring must be studied further before the correlation can be definitely shown.

Newer methods of diagnosis and localization of congenital defects have become more pertinent with the progress in the surgical treatment of these malformations It is incumbent upon the physician to discover if the defect is one which is amenable to surgical treatment. Two technics have found application in this field. These are visualization of the cardiac chambers by the use of radio-opaque substances, and right heart catheterization

Cardiac visualization is achieved by rapidly injecting a radio-opaque material into the antecubital vein and taking a series of x-ray photographs of the heart at short intervals in order to record the passage of the substance through the chambers of the heart and through abnormal openings. All of the exposures of the x-ray films are made within the circulation time which would record the progress of the radio-opaque substance while its concentration is adequate. This test should not be done without good reason, since venous thrombosis occurs at the site of injection with great frequency. Moreover reactions from the test substance may occur. Death has resulted from its use.

In venous catheterization a long catheter is inserted into an arm vein and under

fluoroscopy is passed gradually into the right auricle or right ventricle, or through openings between the auricles or the ventricles, or from the right ventricle into the pulmonary artery out into the lung, or into the coronary sinus or from right ventricle into overriding aorta Intrachamber pressures may be recorded. Samples of blood may be secured at various levels and in various locations in order to determine the oxygen and carbon dioxide contents. These values may be compared with those prevailing in femoral or brachial arterial blood. If the oxygen consumption per minute is measured together with the oxygen contents of the blood from the right side of the heart (mixed venous blood) and of the arterial blood, the application of the Fick principle will permit calculation of the pulmonary and of the systemic blood flows. Ventricular premature contractions and paroxysmal tachycardia have followed the passage of the catheter through a patent interventricular septum to the left side of the heart. Ventricular premature contractions frequently occur with passage of the catheter through the tricuspid valve opening.

Interest in cardiovascular surgery was greatly stimulated by the successful accomplishment of ligation of the patent ductus arteriosus by Gross The anastomosis of a branch of the aorta to the pulmonary artery for the relief of cyanotic heart disease by Blalock resulted from the joint activities of Blalock and Taussig. The independent development of technics for repair of coarctation of the aorta by Gross and by Crafoord took place only a short time apart Richards and Cournand had already laid the foundation for right heart catheterization and Robb and Steinberg for visualization of the cardiac chambers

PATENT DUCTUS ARTERIOSUS

After birth the communication from the pulmonary artery to the aorta, which serves to jump over the pulmonary circuit in fetal life, usually closes and in the course of time becomes fibrous tissue This communicating vessel, known as the ductus arteriosus may, however, remain patent. When this occurs the lumen varies in caliber from a few millimeters up to aneurysmal proportions Without treatment the life expectancy is shortened to about one-half. Roughly 40 per cent of the patients acquire subacute bacterial endocarditis, in about 28 per cent heart failure occurs In a few patients pulmonary aneurysms form which may rupture These last three complications are sufficiently common to warrant the risks inherent in closing the patent ductus surgically There is reason moreover for surgical obliteration of the shunt because of the tremendous burden this defect places upon the heart. The blood volume which is increased in patent ductus arteriosus returns toward normal after operation

Clinical Manifestations

The salient features contributing to the clinical diagnosis are· occasionally a small body build, a lesion more common in girls than in boys, the absence of clubbing of the fingers, the absence of cyanosis, the continuous machinery murmur over the pulmonic area associated with a thrill, the low diastolic blood pressure with a high pulse pressure, the slight left ventricular enlargement, the prominence and enlargement in the pulmonary artery region; increased pulsations in the region of the pulmonary artery and in the pulmonary vessels, the absence of axis deviation

in the electrocardiogram, and the absence of polycythemia. Visualization of the cardiac chambers with a radio-opaque substance may not show the defect. Catheterization of the right side of the heart may yield corroborative evidence. The communication between the high pressure in the aorta and the lower pressure in the pulmonary artery usually increases the pressure in the latter. From the oxygen contents of the blood in the pulmonary artery, in the right auricle, and in the arterial tree the approximate size of the shunt may be calculated.

Selection of Patients for Operation

The operation of closing a patent ductus arteriosus should be recommended to subjects up to 35 years of age. After that age, and if they are in good health, the current opinion is that the defect should not be corrected. Subacute bacterial endocarditis and heart failure are then treated appropriately when they occur. This may be the best course because arteriosclerotic changes in the ductus due to age and to increase in intravascular pressure may make ligation difficult, although a patent ductus arteriosus in a 46-year old man has been successfully ligated by Blalock and a woman 51 years of age by Gross. On the other hand it is usually best not to perform the operation in patients who are too young because of difficulty in arriving at an exact diagnosis in babies. Around 5 to 6 years of age appears to be regarded as the optimal time for operation.

In a few instances of patent ductus arteriosus there is reversal of flow due to increase in pressure in the pulmonary artery so that venous blood flows from the pulmonary artery into the aorta In these cases there is cyanosis of the lower part of the body and extremities with cyanosis and clubbing of the toes but not of the fingers. Difficulty has been encountered in ligation of the ductus in such patients and operation may not be possible.

Operative Details

Closure of the patent ductus is carried out as follows. Ether and oxygen or *cyclopropane anesthesia are given in a closed circuit. The left pleural cavity* is entered anteriorly through the second or third left interspace and the patent ductus is exposed Preliminary compression of the ductus is made to observe its effect on blood pressure and heart rate. The operation is not carried out if other cardiac defects become apparent.

The best procedure dictates *division* of the ductus and suture of the ends when the ductus is of adequate length This is the procedure now recommended by Gross.

Other surgeons resort to *double ligation* of the ductus which, however, may lead to cutting of the vessel by the ligature or an incomplete closure of the shunt, particularly in older patients, when the vessel may be difficult to compress by ligatures. Transfixing sutures are placed between the ligatures.

Heparin is not used after operation. In order to prevent infection, penicillin may be used as in other operations in which the thorax is opened. When the operation is successfully executed the defect is abolished, the abnormal signs and symptoms disappear, and normal circulatory relationships are re-established. Compensation has been restored to patients with heart failure.

Touroff and Gross have advocated the operation in the presence of subacute bacterial endocarditis There is an even chance of survival after ligation. Penicillin would of course be used here too. Subacute bacterial endocarditis may make the vessel friable so that it tears easily, a complication which may render operation difficult. When successful, closure of the ductus results in clearing the blood stream of the offending organisms When subacute bacterial endocarditis is superimposed upon a patent ductus arteriosus, we recommend treatment with appropriate antibiotics, closure of the ductus may then be undertaken at a suitable interval after the endocarditis has been cured. Antimicrobial therapy is continued during the two- to three-month interval If the blood stream cannot be sterilized by antibiotic therapy, operation is indicated without further delay.

The over-all mortality is around 5 per cent. In the hands of the more experienced surgeons the mortality is much lower. For example, the mortality in Gross' series of 412 cases was 2.1 per cent, excluding patients who had complications prior to surgery, the rate was under 0 5 per cent. The course after operation may be surprisingly smooth and without complications, with recovery and discharge from the hospital within two weeks The danger that subacute bacterial endocarditis will occur in later years on the scar from the old healed area resulting from ligation cannot be estimated at present. With penicillin and other agents in reserve this possibility is less formidable.

Care of Patients Not Suitable for Operation

Patients to whom this operation is not recommended as well as those who refuse it should have their activities somewhat restricted, particularly those which give rise to symptoms Respiratory infections should be given proper attention. Penicillin should be used prophylactically before extraction of teeth and tonsillectomy in order to prevent bacteriemia and subacute bacterial endocarditis (Chapter 7) The treatment of heart failure is the same as in other patients. The management of the patient's activities at all ages is similar to that described for rheumatic heart disease.

Pregnancy

While many patients with patent ductus arteriosus appear to sustain pregnancy without embarrassment, because of the increased work of the heart in this congenital defect, to which is added the work consequent to pregnancy and the final increased demand during labor, pregnancy is contraindicated, especially if the estimated size of the shunt is large If the patient is seen before becoming pregnant it might be advisable to recommend closure of the ductus first. If she is seen for the first time after she is pregnant, the patient is allotted the same supervision as that given to patients with rheumatic heart disease The same points should be considered before recommending termination of pregnancy

COARCTATION OF THE AORTA

In the adult type of coarctation of the aorta there is a localized constriction at or just below the insertion of the ductus arteriosus In the infantile type there is narrowing of a longer portion of the aorta, between the left subclavian artery and

the ductus arteriosus. The constriction may be of any degree, from moderate to complete. Coarctation of the aorta is a common defect and is recognized more frequently if the possibility is kept in mind and the blood pressure is recorded in the legs as well as in the arms.

Adult Type

Clinical Manifestations

In coarctation of the aorta the normal relationship between the blood pressure in the arms and legs is reversed, so that the blood pressure is higher in the former, in fact hypertension usually prevails in the arms. There are marked pulsations of the arteries in the upper part of the body, and diminished to absent pulsations from the abdominal aorta downward. Collateral circulation may be detected in the intercostal arteries, scapular, and other vessels—vessels used to bridge the obstruction to the aorta. Over these vessels thrills may be felt and bruits may be heard There may be a systolic murmur and thrill over the base of the heart, transmitted up the neck vessels. There may be a diastolic murmur over the base, transmitted down the left sternal margin, if the aortic ring is widened and the aortic valves are incompetent. There may be enlargement of the heart in the two-meter roentgenogram of the chest. The aortic knob is small and may not be visible. Notching of the lower margins of the ribs by the intercostal arteries occurs in typical cases The electrocardiogram shows left axis deviation Cyanosis and clubbing of the fingers are absent in uncomplicated coarctation of the aorta Visualization of the aorta by intravenous injection of a radio-opaque substance may show the location and extent of the constriction, which provides an indication of the possibility of excision of the constricted area and whether sufficient lengths of aorta will be left to approximate in the end-to-end anastomosis Retrograde filling of the aorta with the radio-opaque material through the carotid artery may visualize a constriction which might not be seen following its intravenous introduction. The ballistocardiogram may be abnormal

It is necessary to make the diagnosis of coarctation of the aorta for the following reasons (1) recognition of this defect as the cause of hypertension, in order that these patients be spared lumbodorsal sympathectomy as a treatment for the hypertension, (2) in order to advise the patient and relatives how the patient should live, (3) because of its association with subacute bacterial endocarditis, (4) because of the tendency to cerebral aneurysms, (5) because of the frequent occurrence of aneurysmal dilatation of the aorta and because of the tendency of the aorta to tear and rupture, (6) because patients may have heart failure, and finally (7) because both Gross and Crafoord have devised technics for resection of the constricted area in suitable cases in order to correct the defect, a procedure resulting in reversal of the blood pressure pattern so that normal relationships are restored

Many patients exhibiting this defect may look forward to long active lives; others have shortened life expectancies and may experience any of the complications which have just been mentioned. The aortic valve may be bicuspid

Selection of Patients for Operation

Present experience would indicate that patients should not be chosen for surgical excision of the constricted area after the second decade, with the ages 15 to 20 being the most suitable. After this period arteriosclerotic changes in the aorta from aging and from the effects of hypertension tend to make approximation and suture of the transected aorta impossible. If the age of the patient is chosen correctly the ring of scar tissue at the point of suture—which will not increase in diameter as the patient grows—will be of sufficient size to prevent the subsequent development of a new area of constriction. Patients over 20 years of age, however, have been successfully operated upon

In certain younger patients with marked hypertension early operation might be indicated to relieve the hypertension, a second operation might be done some years later if it became apparent by recurrence of hypertension that the lumen of the aorta at the suture line of the earlier operation had not enlarged proportionally with growth of the individual

Technic of Operation

The aorta with the area of constriction is exposed in a transthoracic approach A clamp is placed above and below the constriction and the constricted area is resected The transected ends of the aorta are then brought together and an end-to-end anastomosis is made with a continuous mattress suture Gross recommends that the lower clamp be removed first and the upper one slowly over a period of about ten minutes, a precaution which Crafoord does not think necessary Clamp-

not given. If a large segment of the aorta must be resected it may not be possible to draw the two ends of the aorta together without too much tension on the suture line In a few such instances the removed segment has been replaced by an appropriate arterial transplant from a blood vessel bank. The aorta has been sutured with fine silk, which being nonelastic may account for the development of a new constriction if the operation is carried out before the aorta has achieved its optimal normal growth It has been suggested that absorbable sutures would eliminate this drawback

If the ductus arteriosus is patent it is ligated before resecting the coarctation

Postoperative Course

Convalescence may be smooth with mobilization in a week to ten days. We have

the lower part of the body which had been so long accustomed to a reduced flow. Although this operation has been developed too recently for us to know its final effect upon the life history, with correction of the anatomic defect patients should look forward to a normal span of life if (1) approximation of the two ends of the

aorta occurs with a strong union, (2) irreversible changes in vessels and organs have not occurred, and (3) restoration of normal blood pressure relationships occurs.

Infantile Type

Johnson and Kirby have devised an operation for the correction of the defect in patients with the infantile type of coarctation of the aorta, in which there is an elongated narrowing of the aorta at the isthmus. They have divided the subclavian artery and rotated it downward to bridge the defect by an end-to-end anastomosis with the descending aorta, after the area of defect had been excised. Blalock and Park had earlier used this procedure in the correction of coarctation of the aorta. The criteria for selection of patients is the same as in the adult type

Coarctation Associated with Aneurysm

Alexander and Byron reported the history of a patient in whom an aneurysm of the aorta associated with coarctation of the aorta was treated by excision and ligation of the distal and proximal ends of the aorta. The patient survived the operation but died several months later. Autopsy was not obtained. In this patient permanent transection of the aorta was possible because the collateral circulation had already been prepared by the presence of the coarctation, so that blood from above the section could enter the aorta below the section by these bridges.

Schumacker has recently reported the excision and successful end-to-end repair of the aorta in a patient whose coarctation was associated with an aneurysm distal to the stenosis In this instance the ends of the aorta could be adequately mobilized and approximated even though 2.5 to 3 cm. of the aorta was removed Recovery was uneventful and the blood pressure in the arms and legs assumed normal proportions and relationships About six weeks earlier this patient had bacteriemia—probably from infected vegetations within the aneurysmal sac—which subsided with the use of penicillin and sulfadiazine.

These two cases are cited to demonstrate how much surgery may contribute to the treatment of congenital defects of the heart and the blood vessels. In the future it might be possible to replace the resected portion of the aorta by a segment of appropriate length from a blood vessel bank.

Care of Patients Not Suitable for Operation

Because of the hazard of rupture of the aorta patients exhibiting coarctation of the aorta who are not suitable for operation should avoid prolonged exertion and straining, and sudden demands on the heart which the lifting of heavy objects requires. When the diagnosis is made in childhood, patients should be guided early into suitable occupations; adults, too, should be advised about the type of work which is suitable The teeth should have good care. Penicillin prophylaxis should be used when extraction of teeth and tonsillectomy are required. Respiratory infections should be treated promptly. When heart failure occurs it is treated as in other patients suffering from cardiac decompensation

When subacute bacterial endocarditis is superimposed on the defect of coarctation of the aorta it is treated in the usual manner.

Rupture or tear in the aorta may occur slowly Death usually occurs within a few

days The prognosis in coarctation of the aorta is guarded; a patient in apparent good health may succumb suddenly to rupture of the aorta or of a cerebral aneurysm.

Pregnancy in Patients with Coarctation

Women with coarctation of the aorta should not become pregnant. This is especially the case if the blood pressure is much elevated When advice is sought about the advisability of pregnancy, the risks which are incurred may be explained to the patient and her husband, if they are insistent, so that they can be prepared to assume them. The management of pregnancy in patients with this congenital defect is discussed in Chapter 28 It is well to bear in mind that even though many of these patients suffer no apparent harm from labor, the effect of the strain cannot be predicted. The appearance of signs of aortic insufficiency after childbirth and its persistence are evidences of the irreversible distension of the aortic ring

CONGENITAL PULMONARY STENOSIS

Tetralogy of Fallot

It is for patients with the combination of defects known as the *tetralogy of Fallot* that the Blalock-Taussig operation was devised. The following combination of lesions constitutes this condition: (1) pulmonary stenosis or atresia, (2) interventricular septal defect which is located high in the septum; (3) dextroposition of the aorta, although the aorta arises from the left side it overrides the septal opening and receives a certain amount of blood from the right ventricle, and (4) marked right ventricular hypertrophy due to the pulmonary stenosis and to the dextroposition of the aorta.

Pathologic Physiology

Two factors contribute to the marked cyanosis which these patients exhibit (1) a certain amount of venous blood is discharged directly into the aorta and enters the arterial system; (2) venous blood pours through the interventricular septal defect into the left ventricle, because the pulmonary stenosis increases the pressure in the right ventricle The blood shunted from the right ventricle mixes with the oxygenated blood of the left ventricle and reduces its oxygen content When this blood enters the aorta, it is further diluted with venous blood which is discharged directly into the aorta On the other hand, the amount of blood which is expelled into the pulmonary artery with right ventricular systole is reduced because of the pulmonary stenosis As a consequence the volume of blood which returns to the left auricle and left ventricle as oxygenated blood is diminished. The average oxygen saturation of the blood in the aorta for delivery throughout the body may be reduced to such low levels as 30 per cent. Compensatory polycythemia results There is great increase in the circulating blood volume, due for the most part to increase in the number of red blood cells, the plasma volume usually being below the expected amount.

Venous catheterization shows that the systolic pressure in the right ventricle is increased and may approximate that of the peripheral arterial system. The oxygen

content of the right ventricular blood is higher than that of the right atrium due to left to right shunt through the ventricular septal defect. The oxygen content of blood samples from the left auricle would be normal and therefore high, on the average blood from this chamber would be approximately 95 per cent saturated as it leaves the pulmonary vein The oxygen content of arterial blood would be lower than that in the left auricle because it would be diluted with not only the venous blood which enters the left ventricle by the shunt but also by that which enters the aorta directly From data supplied by the oxygen consumption of the patient per minute and the oxygen contents of these samples of blood, the Fick principle may be applied in the calculation of the pulmonary and systemic blood flows. It turns out that the pulmonary blood flow is greatly decreased and that the systemic blood flow approximates the normal level.

Clinical Manifestations

Cyanosis is usually extreme. Clubbing of the fingers and toes may be marked There may be a systolic murmur as well as a systolic thrill along the left sternal margin The heart may not be greatly enlarged The pulse pressure is small. There is right axis deviation in the electrocardiogram and increased amplitude of the P waves On fluoroscopic examination the heart is usually of normal size or only slightly large, there is absence of fullness in the region of the pulmonary artery, there is no hilar dance The lung fields are of decreased density due to decrease in pulmonary circulation. Approximately one-fifth of the patients have a right aortic arch which is demonstrated on fluoroscopy and in x-ray photographs taken after a barium swallow. Exercise makes the cyanosis more marked because the arterial unsaturation is increased.

The intravenous injection of a radio-opaque substance shows simultaneous visualization of the aorta and pulmonary artery, unless the pulmonary stenosis is so marked that the amount of blood which can enter the pulmonary artery is greatly reduced Shunting of blood from the right to the left ventricle through the septal defect may or may not be seen.

Patients with tetralogy of Fallot may have a moderately good functional capacity, they may be so handicapped that they can take only a few steps, or they may be invalids. Heart failure however is uncommon. They are subject to attacks of transient paralysis Because of the polycythemia and the high viscosity of the blood they may suffer thromboses, especially of the cerebral vessels. They may suffer from subacute bacterial endocarditis.

Blalock-Taussig Operation

The operation of Blalock and Taussig is designed to increase the circulation through the lungs and to provide for the body a greater amount of oxygenated blood. This is achieved by recirculating the mixed venous and arterial blood contained in the aorta through the lungs. An anastomosis between a branch of the aorta and one of the pulmonary arteries achieves this. A branch of the aorta is selected of a size that will make an adequate correction for the decrease in pulmonary flow. The vessel which is selected should not convey more blood to the

lungs than can be accommodated by their vascular tree. If too large a volume of blood is poured from the aorta into the lungs, pulmonary edema will occur.

TECHNIC. Under cyclopropane anesthesia with high concentration of oxygen, exposure is usually made on the right side. In those instances in which a barium swallow has shown that the innominate artery arises on the left side, the operative approach is made from the left. Since about one-fifth of the patients with tetralogy of Fallot have right aortic arches, it is necessary to have ascertained from x-ray photographs or fluoroscopy after a barium swallow whether the arch descends on the right or on the left. The chest is entered on the side opposite the arch. With this exposure, the innominate, the subclavian, or the carotid artery is available for use, subclavian being used most commonly, the innominate artery the next most suitable vessel. The end of the systemic artery is anastomosed to the side of the pulmonic artery so that additional circulation is conveyed to both lungs.

Because of polycythemia, patients should have *adequate fluids* and should not be dehydrated before operation During operation a slow intravenous infusion restores fluids as they are lost and makes this channel available for plasma infusion if there is loss of blood during the operation Plasma is used sparingly in order not to pull too much fluid into the blood stream. If the operation has been accomplished without blood loss and polycythemia is marked, blood may be removed by venesection with benefit at the end of the operation Oxygen is provided postoperatively A fluid intake suitable for the age of the patient is insured by the intravenous route until fluids are taken by mouth

Anticoagulants are not used unless hemiplegia occurs With the latter complication, heparin is more efficacious than dicumarol because of its more rapid action Hemiplegia occurs more commonly when the innominate or common carotid artery is used for the shunt than when the subclavian artery is employed

Pneumothorax, pleural effusion, and heart failure are treated by appropriate means

SELECTION OF PATIENTS FOR OPERATION. If the diagnosis of congenital pulmonary stenosis with patent interventricular septum is made in infancy it is best to delay surgical treatment until the patient is around two years of age By this time the vessels may attain calibers which make accomplishment of the Blalock-Taussig procedure easier Patients up to 15 years of age are considered to be in the optimal age range Blalock and Taussig are of the opinion that the optimal time for operation is between the age of 5 to 10 years On the other hand, many patients in their early twenties have been operated upon A patient whom I first saw when he was 20 years old was successfully operated upon at 43 years by Blalock There are, of course, inherent dangers in carrying out this operation on such a subject: In the first place, arteriosclerotic changes in the vascular tree with aging may increase the difficulty in making the anastomosis In the second place, the lungs may not adapt so easily to the sudden increase in pulmonary circulation

The indications for operation are the degree of incapacity of the patient and the magnitude of the polycythemia and of the hematocrit value Patients suffering from the *Eisenmenger complex* are not suitable for the Blalock-Taussig operation. This complex is characterized by patent interventricular septal defect, right-sided or overriding aorta, and right ventricular hypertrophy with dilatation of the pulmonary

artery rather than the pulmonary valvular or infundibular stenosis which occurs in *tetralogy of Fallot.*

POSTOPERATIVE COURSE AND PROGNOSIS. Although serious complications may occur after this operation, the postoperative course in most patients is smooth. Patients are ambulatory in seven to ten days and are ready to go home in two to three weeks When patients experience maximal benefit cyanosis disappears, the lips assuming a normal color, although residual cyanosis of the nail beds may persist, clubbing of the fingers and toes regresses; the red blood cell count, hemoglobin, and hematocrit decrease to normal levels; and the oxygen saturation of the arterial blood rises to 80 per cent or more. The functional capacity of the patient is greatly augmented.

Nearly three-quarters of the operated patients have been greatly improved. With clearer delineation of the limits of the operation the mortality may be approximately 15 per cent

The benefit of the Blalock-Taussig procedure is achieved by the artificial induction of a ductus arteriosus. A communication is made so that arterial blood which has an oxygen saturation less than the normal value enters the pulmonary artery and recirculates through the lungs Owing to the pulmonary stenosis the amount of blood entering the pulmonary artery to circulate through the lungs and attain oxygenation is decreased. As a result of this operation an additional amount of blood is shunted into the pulmonary artery above the stenosis. Consequently the volume of oxygenated blood returning to the left side of the heart is increased and its saturation is raised so that it ranges from 70 to 90 per cent. Additional oxygen is thereby made available to the body. The systemic blood flow is increased. This operation does not alter the circulation in the right ventricle; the pulmonic stenosis, the interventricular septal defect, and the overriding aorta remain.

The fact that a second artificial defect has been created by the Blalock-Taussig operation in a patient with multiple congenital defects does not provide an argument against the operation. By this procedure the summated pathologic physiology is converted into one which provides a more appropriate physiologic mechanism for supplying the bodily requirements for oxygen. In short, it relieves the cyanosis although it also increases the work of the heart, which is thereby subject to the consequences of this increased work, namely possible left ventricular hypertrophy and heart failure Observation of operated cases over a long period of time will be required in order to estimate in each instance how well the handicaps of one combination of lesions has been overcome by another artificial lesion which has consequences of its own.

RESULTS. From Blalock and Taussig's large series it appears that a patient with tetralogy of Fallot has an 85 per cent chance of surviving operation with great improvement, and of maintaining the improvement. After recovery from operation, the additional artificial defect does not appear to increase appreciably the susceptibility to subacute bacterial endocarditis.

It must be kept in mind however that even with great improvement patients are not "cured" The patient is not relieved of the hazard of subacute bacterial endocarditis nor of the potential danger of heart failure.

Anastomosis Between Aorta and Pulmonary Artery

In 1948 Potts, Smith, and Gibson reported another operative procedure for the treatment of the tetralogy of Fallot. They accomplished a *direct anastomosis* between the aorta and the pulmonary artery This was made possible by the development of a special clamp which pinched off a pouch on the side of the aorta through which an anastomosis could be effected with the pulmonary artery while blood passed through the remaining tube of the aorta to maintain the circulation

Valvulotomy (Brock)

Brock has carried out valvulotomy for the pulmonary valvular stenosis in Fallot's tetralogy. He has reported benefit from this procedure. He is of the opinion that, since it relieves the strain on the right ventricle, it does not put the strain on the left ventricle which the Blalock-Taussig procedure incurs The final decision of the best procedure will come from a long time follow-up of the patients subjected to these two procedures. In certain of these patients he resected or dilated infundibular stenosis, which was the lesion instead of valvular stenosis

Pulmonic Stenosis with Intact Interventricular Septum

Brock has described the following anatomical variations: (1) pure valvular stenosis; (2) pulmonary artery hypoplasia and valvular stenosis; (3) high infundibular stenosis with normal pulmonary valves; and (4) low infundibular stenosis with normal pulmonary valves

In pulmonic stenosis with an intact interventricular septum experience has shown that the Blalock and Taussig operation is contraindicated In the series of these two investigators, all the patients who survived the operation developed "right-sided" heart failure Enlargement of the pulmonary valve opening by surgical means is now the approach which is recommended.

Valvulotomy

In June, 1948, Brock first reported pulmonary valvulotomy for the correction of congenital pulmonary valvular stenosis Since then he has enlarged his series of cases Blalock and Taussig and Glover, Bailey, and O'Neill have also reported on *their experience with the Brock operation* For pure valvular stenosis Brock recommends dividing the valve into two equal cusps by using a special knife inserted through the right ventricle. When infundibular stenosis is suspected, the right ventricular chamber is entered either proximal or distal to the obstructing septum and by means of a backward cutting punch a collar of tissue is excised. In either case the ventricular incision is closed with interrupted silk sutures

The improvement to exercise tolerance has been striking. The preoperative polycythemia disappears, the arterial oxygen saturation increases,—both of which are present only if the foramen ovale is patent—and the low pulmonary artery pressure prevailing before valvular division has risen to the normal range at the end of the procedure

MARFAN'S SYNDROME

The presence of congenital cardiac defects and their complications should be borne in mind in patients with Marfan's syndrome. This syndrome is a familial symptom complex characterized by arachnodactyly (spider fingers), congenital bilateral dislocation of the lenses, and congenital or acquired cardiac abnormalities. There may be other associated congenital malformations. The cardiovascular lesions include aortic medial necrosis and endocardial lesions which simulate those of rheumatic fever. The aortic medial necrosis may lead to sudden death due to dissecting aneurysm and rupture of the aorta.

DOUBLE AORTIC ARCH

When a double aortic arch occurs the ascending aorta divides into two branches, the posterior portion passing behind the trachea and esophagus and the anterior portion in front. They then unite to form the descending aorta. The trachea and esophagus are surrounded by the split aorta, which forms a ring This may give rise to symptoms of compression: Noisy, stridulous breathing and difficulty in swallowing occur; solid foods cause distress. Patients are prone to upper respiratory symptoms and in later life bronchiectasis may occur. Diagnosis is made by bronchoscopic examination and by x-ray photographs taken after spraying lipiodol into the trachea and after a barium swallow. Relief from constriction is accomplished by surgical section of the smaller branch, which is usually the anterior. If patients can be maintained past the first few months, the symptoms often become less and finally disappear without operation.

BICUSPID AORTIC VALVES

Bicuspid aortic valves are important principally as fertile soil for subacute bacterial endocarditis The possibility of this defect should be considered when subacute bacterial endocarditis with predominant aortic involvement occurs in a heart which was previously thought to be normal, or in a heart in which the signs are predominantly aortic, and history of previous rheumatic fever or obvious congenital cardiac defects is absent Because the cusps approximate accurately in most instances of this defect, murmurs are not usually heard until subacute bacterial endocarditis occurs They may occur with coarctation of the aorta

There is no corrective therapy.

UNCOMPLICATED CONGENITAL DEXTROCARDIA

Patients with uncomplicated congenital dextrocardia have normal cardiac function and live a normal life span. They are subject to the same diseases as are individuals with normally placed hearts There may be complete transposition of the heart and abdominal viscera known as *situs inversus*, or only the heart may be transposed These anomalies are of the mirror type, in that the usual left chambers lie on the

right side and form the right cardiac margin and the apex and the right chambers lie on the left. When the dextrocardia is isolated there may be other congenital cardiac anomalies *The electrocardiogram is also of the mirror type in congenital* dextrocardia: the complexes in Lead I appear inverted and Leads II and III transposed.

Patients with situs inversus appear to be more susceptible to bronchiectasis than individuals with normally placed hearts With this exception, patients with uncomplicated dextrocardia have no unusual predispositions and require no special treatment.

CONGENITAL HEART BLOCK

Congenital heart block may be complete or it may be high grade. In the latter type a 2:1 or 3:1 ratio occurs, with two or three auricular beats to each ventricular contraction. On occasions the block may not be fixed but may vary between incomplete and complete auriculoventricular dissociation The ventricular rate may be more rapid in complete heart block of congenital origin than it is in the acquired type Patients with no other congenital defects, such as atrial or septal communications, may lead normal lives provided they avoid overexertion Female patients may be allowed to go through pregnancy if they have no evidence of decreased functional capacity The management and treatment of the consequences of congenital heart block are given in Chapter 5

WOLFF-PARKINSON-WHITE SYNDROME

The Wolff-Parkinson-White syndrome is an electrocardiographic finding characterized by a short P-R interval and a long QRS time It is probably a congenital defect of the conduction system, and may be associated with other congenital defects of the heart, especially interventricular septal defect Patients having this defect are prone to attacks of paroxysmal tachycardia which may be difficult to terminate When paroxysmal tachycardia unusually difficult to control is encountered, the presence of this syndrome should be considered Its treatment is discussed in Chapter 5

NONSURGICAL MANAGEMENT OF CONGENITAL CARDIAC DEFECTS

A large number of patients have congenital cardiac defects which are not amenable to correction or conversion into less disabling defects, or they may not be suitable for operations or may refuse them For these persons careful supervision, limitation of activities to the extent compatible with their functional capacities, and good medical care are the only measures available For the most part the supervision at all ages is approximately the same as the regimen and principles given under rheumatic heart disease In the cyanotic patient with polycythemia an occasional phlebotomy may prevent thromboses.

SUMMARY

Interest in congenital heart disease has taken on great dimensions. A fortunate set of circumstances has been responsible for this. Gross selected a lesion, patent ductus arteriosus, which, once the barrier to surgical treatment had been lifted, was relatively simple to cure by surgical means, and could be performed with a minimal degree of operative mortality. Subsequently, with experimental work on animals and experience with patients, surgeons became capable of more radical procedures. As a part of this trend, Blalock and Taussig developed an approach to the treatment of the cyanotic types of congenital heart disease which has been used successfully by them and by others. Then came the simultaneous operations of Gross and of Crafoord for the correction of coarctation of the aorta. Finally Brock contributed the technic of valvulotomy for the treatment of congenital pulmonary stenosis.

In these four major surgical contributions there has been progression from a relatively simple operation for the cure of patent ductus arteriosus to a more complex one involving the anastomosis of an artery to the pulmonary artery in the treatment of tetralogy of Fallot, and finally to one which requires perhaps greater courage and skill, the transection of the aorta. These fruitful investigations have stimulated other surgeons to explore the use of other procedures. There were available, waiting for application when the time was propitious, two diagnostic technics which have been of help visualization of the cardiac chambers and right heart catheterization. These procedures were major ones to which it did not appear appropriate to subject patients for diagnosis if corrective therapy was not available. With surgical operations available for certain of these defects, it has become incumbent upon physicians to establish or rule out the diagnosis of those lesions susceptible to benefit by surgical means. During all this time a great volume of information relating to the pathologic physiology in congenital defects of the heart has been built up. No doubt the congenital lesions of the heart which will come into the province of cardiac surgery will be greatly expanded if the experiments directed at supplying an extracorporeal circulation achieve success, so that the internal chambers of the heart and the valves may be operated upon under direct vision

Finally there has been one more development in internal medicine which is important to patients with congenital cardiac disease: the cure of subacute bacterial endocarditis by the use of penicillin and of other antimicrobial agents

These major advances in the treatment of congenital heart disease in the last decade should give encouragement to physicians to look forward with eagerness and confidence to future developments.

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CHAPTER 7

Rheumatic Fever and Rheumatic Heart Disease

RHEUMATIC FEVER

Rheumatic fever is a disease of unknown etiology essentially chronic in course showing acute phases and a tendency to recurrences. Rheumatic fever is often, if not invariably, initiated by a beta hemolytic (Group A) streptococcal infection, generally occurring two to three weeks before the onset of the disease. The exact mechanism by which the streptococcal infection, alone or with other factors, precipitates rheumatic fever is not clear.

The typical myocardial lesion, the Aschoff body, is pathognomonic of the disease A specific cure for acute rheumatic fever is not known.

Clinical Course

Typically, the patient suffers an acute upper respiratory infection or acute tonsillitis during which beta hemolytic (Group A) streptococci may be isolated from throat cultures Two to three weeks later the patient falls sick again, now with rise in temperature, increase in pulse rate, malaise, and migratory polyarthritis. The joints are red, swollen, tender, and painful on motion, and the synovial spaces may become distended with fluid There is moderate leukocytosis and increase in sedimentation rate During the active stage of rheumatic infection the antistreptolysin-O titer of the blood may be elevated.

The joint manifestations may subside promptly without the appearance of other manifestations or there may be cardiac involvement. In the latter case the disease may be prolonged for many weeks or months Valvular damage may persist after recovery or may become manifest for the first time months or years after the initial infection Rheumatic nodules may appear on the tendons of the hands and feet, at the elbows, wrists, knees, and in the scalp, proliferative manifestations which

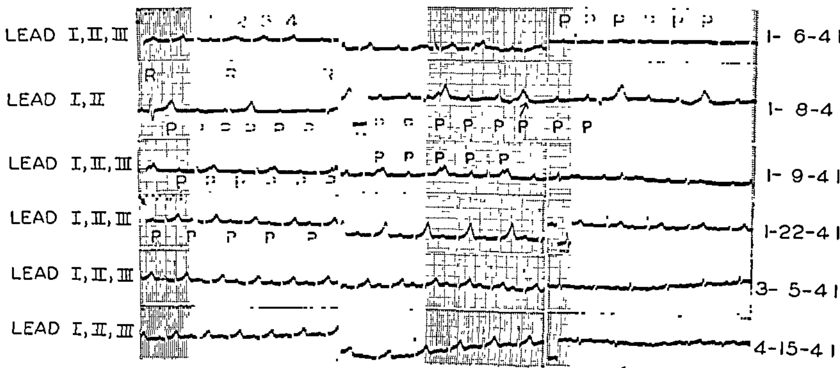


Fig. 35.

Auriculoventricular Conduction Changes Which May Occur During Active Rheumatic Carditis.

Subject was a boy 18 years of age Electrocardiogram taken *January 6, 1941* showed incomplete heart block with Wenckebach phenomenon. In complex 1 (in Lead I) P-R time is 0 20 sec, in complex 2 P R time is 0 22 sec; in complex 3 it is 0 27 sec., and at 4 P and T waves are superimposed and P wave is blocked, excitation wave not going down to ventricles In Lead II P-R time is again short and followed by progressive lengthening until a P wave is blocked *In Lead III* P waves are identified by "P", 5th P wave is blocked, and pattern starts over again. An artefact is shown between second and third R waves in Lead II.

January 8 Complete heart block present Auricular rate 111, ventricular rate 33 per minute Complete dissociation of auricular waves (PPP) and QRS complexes (RRR), with idioventricular rhythm, normal conduction occurs, however, in first QRS complex in Lead I, and first and third QRS complexes in Lead II.

January 9: 2:1 heart block, two P waves (PPP) to one QRS complex P R time 0.36 sec in Lead II in conducted beats.
January 22: first degree block present, P-R time now 0.31 sec The P waves indicated (PPP) in Lead I
March 5: P-R time has decreased to 0.25 sec.
April 15. restoration of normal conduction time of 0 12 to 0 16 sec. in Lead II

Accordingly there was first incomplete heart block with Wenckebach phenomenon, then complete heart block, then 2:1 heart block, then first degree heart block, that is to say, prolongation of P-R time, which decreased to a normal value

presage a severe infection. There may be evidence of pulmonary involvement, with signs of pneumonitis or of acute pleurisy with effusion. Skin rashes may occur.

Patients may recover from the acute infection with no residual evidences of activity. Other patients suffer cyclic recurrences or evidences of low-grade rheumatic activity which persist for many months. Chorea may occur alone without any other evidence of rheumatic infection or may occur with polyarthritis with or without carditis. Although chorea may persist for many months it is now considered a relatively mild manifestation of rheumatic activity.

Cardiac Involvement

Cardiac involvement of the myocardium, endocardium (valvulitis), or pericardium may occur alone or in varying combinations.

The *myocardial* involvement is manifested by tachycardia, by change in character of the heart sounds with perhaps a gallop rhythm, by enlargement of the heart or by the onset of acute heart failure. The electrocardiogram may show alterations in T waves and in P-R conduction time (Fig. 35). Irregularities of rhythm may occur. auricular fibrillation, auricular flutter, paroxysmal tachycardias, and premature contractions. Patients may complain of precordial pain. If the anatomic changes are extensive, alteration in the functional capacity of the heart occurs, with the appearance of heart failure *Endocardial* involvement may be detected by the appearance of murmurs which may undergo changes from day to day. In the acute stage it is unlikely that enough change in the structure of the valves occurs to bring about alterations in functional capacity of the heart. If however, there is concurrent myocardial damage, the defect in the valves becomes more important in the maintenance of an adequate circulation. After valvular damage becomes established, either by single or repeated attacks of rheumatic infection, compensation may be maintained until further bouts of activity of the rheumatic process increases the load to the point at which the heart can no longer maintain an adequate output.

Pericardial involvement is associated with precordial pain, onset of or increase of dyspnea, increase in heart rate, pericardial friction rub, and typical changes in the conformation of the T waves and RS-T segments The presence of pericardial effusion may be suspected when percussion or x-ray shows an increase in heart size, when the heart sounds fainter, and when the venous pressure rises with evidence of cardiac tamponade.

Incidence

Rheumatic infections in children lead to more cardiac and fewer joint manifestations than in older subjects The disease occurs occasionally in very young children, the incidence increases so that the mode or greatest incidence is around 11 years of age The incidence then falls off in the middle decades Patients may have only a single attack, but it is common to have recurrences year after year until adolescence After this period the frequency of recurrences decreases.

Rheumatic fever is more common in females than in males

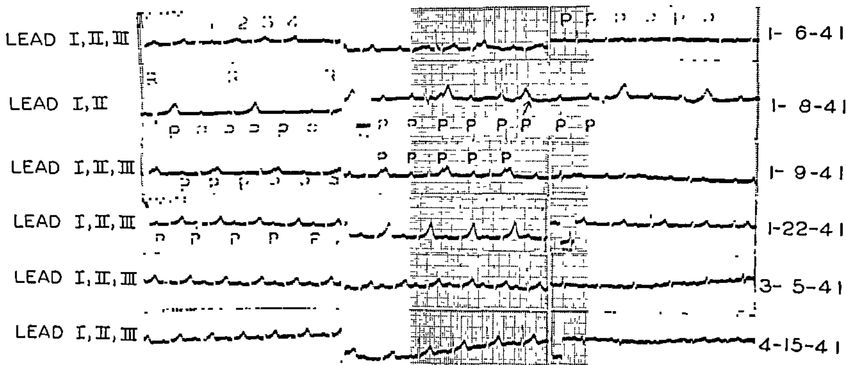


FIG 35.

Auriculoventricular Conduction Changes Which May Occur During Active Rheumatic Carditis.

Subject was a boy 18 years of age Electrocardiogram taken January 6, 1941 showed incomplete heart block with Wenckebach phenomenon. In complex 1 (in Lead I) P R time is 0 20 sec, in complex 2 P-R time is 0 22 sec; in complex 3 it is 0 27 sec; and at 4 P and T waves are superimposed *and P wave is blocked*, excitation wave not going down to ventricles In Lead II P-R time is again short and followed by progressive lengthening until a P wave is blocked In Lead III P waves are identified by "P", 5th P wave is blocked, and pattern starts over again An artefact is shown between second and third R waves in Lead II

January 8 Complete heart block present Auricular rate 111, ventricular rate 33 per minute Complete dissociation of auricular waves (PPP) and QRS complexes (RRR), with idioventricular rhythm, normal conduction occurs, however, in first QRS complex in Lead I, and first and third QRS complexes in Lead II.

January 9 2:1 heart block, two P waves (PPP) to one QRS complex P-R time 0 36 sec in Lead II in conducted beats.
January 22: first degree block present, P-R time now 0.31 sec The P waves indicated (PPP) in Lead I.
March 5: P-R time has decreased to 0.25 sec.
April 15 restoration of normal conduction time of 0 12 to 0 16 sec in Lead II.

Accordingly there was first incomplete heart block with Wenckebach phenomenon, then complete heart block, then 2 1 heart block, then first degree heart block. that is to say, prolongation of P R time, which decreased to a normal value.

60 Gm. daily, divided into six fractions The white blood cell count must be followed frequently to detect granulocytopenia Amidopyrine does not cause gastric symptoms or other signs of salicylism and sodium bicarbonate is not required.

Alternate and Experimental Therapy

1. *Cinchophen* or *neocinchophen* may be used but neither is recommended because of possible liver damage

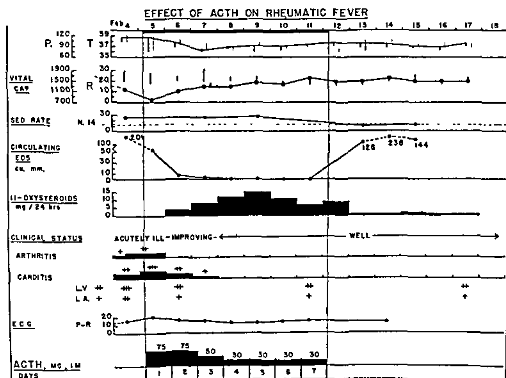


Fig 36

Data Relating to the Effects of ACTH

The patient, a boy 8½ years of age who had an attack of acute rheumatic fever with cardiac involvement, was cured within a few days, suffered no relapse, and has been well since that time (Wilson, May G., and Helper, Helen N Effect of pituitary adrenocorticotropic hormone (ACTH) in acute rheumatic carditis J.A.M.A 145 133, 1951)

2 Experience has shown that neither *penicillin* nor the *sulfonamides* are of benefit in treatment of acute rheumatic fever after its onset.

3 Gubner and Szucs have recently suggested the use of the *calcium double salt* [illegible]

[illegible] responded more favorably than those treated with salicylates. On the other hand Wégria, Fischel, and Wilson were unable to detect any benefit from the use of a succinate compound.

TREATMENT OF RHEUMATIC FEVER

The treatment of rheumatic fever and rheumatic heart disease concerns itself with (1) the treatment of the acute phase of the disease, (2) the care of rheumatic fever patients after episodes of active infection, and (3) the treatment of patients who acquire rheumatic heart disease.

Acute Rheumatic Fever

1. The patient should be at complete rest in bed. The pulse, temperature, and respirations should be recorded about four times a day.

2 The *diet* should be well balanced. A high caloric intake is recommended when it can be taken. Vitamin supplements may be used.

3. *Mild laxatives* should be used when necessary to obtain daily bowel movements.

4. *Fluids* should be forced, to be certain of an adequate fluid intake, unless there is evidence of heart failure.

5 *Salicylate* in the form of aspirin (acetylsalicylic acid) or sodium salicylate, should be given in doses sufficient to lower the temperature and alleviate the joint manifestations. Five to ten grams daily, divided into six doses at four-hour intervals together with sodium bicarbonate in half the dose of the salicylate are usually sufficient. The drug is best tolerated after meals, or after crackers and milk It is unnecessary to give the drug to the point of toxicity. Nausea and vomiting should be treated by reduction of the salicylate or increase of the sodium bicarbonate If hyperventilation with alkalosis occurs the drug should be discontinued. Tinnitus, however, is often the accompaniment of doses essential to control the disease, but generally it becomes less bothersome after the patient has taken the drug for three to seven days. At present there is no evidence that massive doses of salicylate orally or intravenously—which have resulted in salicylate poisoning and death—cure rheumatic infection or prevent the cardiac complications.

Coburn recommends 10.0 Gm. daily with the idea of maintaining the blood level at 35.0 mg per cent. When the usual dosage is given it is generally not necessary to estimate the blood level If the patient is not responding satisfactorily to the drug or if very large doses are necessary, salicylate blood levels should be estimated to ascertain whether the salicylates are being absorbed and to be certain that the blood level is not excessive.

Sodium salicylate may be given in doses of 3.0 to 4.0 Gm. *by rectum* in 150 to 200 cc. of warm starch water, three or four times a day, if the patient has nausea and vomiting and cannot retain the salicylates given orally. Since salicylates by mouth are rapidly absorbed, nothing is gained by giving the drug *intravenously*. Moreover the latter procedure may be dangerous

The acute exudative manifestations of acute rheumatic fever are dramatically alleviated by salicylates, but the proliferative manifestations are unaffected. Salicylate therapy relieves symptoms but there is no evidence that it alters the course of the disease.

6. If salicylates are not tolerated, *amidopyrine* may be given in doses of 2.0 to

carditis Wilson recommends an initial daily amount of 80 to 100 mg of ACTH (20 to 25 mg. every six hours) for the first three days and 40 to 60 mg. daily for the next four days; during therapy the circulating eosinophiles should probably be maintained at zero levels A failure to drop to zero levels or a rise during treatment probably indicates inadequate dosage. When adequate dosage has not been initially presented there is an escape of the circulating eosinophiles, rise in the sedimentation rate, and reappearance of signs of activity which may require a second exhibition of the drug

Spontaneous diuresis occurs 24 hours after discontinuance of the drug. Even though there may be evidence of effectiveness of the drug, murmurs may appear during treatment. When larger amounts of the drug are used it may be necessary to administer potassium chloride to replace the potassium, whose loss gives rise to weakness. This should be done with care in order not to induce potassium intoxication. When ACTH is given for these short periods hypertension or toxic symptoms are not to be expected

In titrations of the effectiveness of cortisone and of ACTH in rheumatoid arthritis it appears that 40 mg. of ACTH are equivalent to 100 mg. of cortisone. In active rheumatic fever Hench and his associates recommend that 200 mg. cortisone intramuscularly or about 60 mg ACTH be given daily for suppressive effects for 10 to 20 days followed by 100 mg. or 30 mg. respectively for maintenance doses for one or two weeks.

The mechanism of the action of these compounds in terminating the activity of rheumatic infection is at present unknown Determination of their place in the routine treatment of patients with active rheumatic infection awaits further investigation

6 Massell, Warren, Patterson, and Lehmus have reported the antirheumatic activity of ascorbic acid in large doses in a few patients They gave 1 0 Gm four times a day for eight to twenty-six days. They reported disappearance of joint manifestations, fall in temperature, slowing of the heart rate, and improvement in the general condition The sedimentation rate did not fall to normal in all patients There were no apparent toxic effects. This was a small series of cases and the follow-up was short It remains for subsequent study to show whether the early hopes about these preliminary results are fulfilled The mechanism of action of vitamin C in this disease is unknown

Course During Treatment

In the great majority of patients with rheumatic fever, the temperature falls to normal in 24 to 48 hours after the administration of adequate doses (5 0 to 10 0 Gm) of a salicylate The joint pains subside and swelling of the joints (fluid in cavity) decreases The patient feels better and looks much improved. The white blood cell count often falls to normal in one to two weeks The sedimentation rate is slower in returning to normal and may become stabilized at a high level for months or for a year or more.

The drug is given until all signs and symptoms of active infection have subsided. The sedimentation rate should have returned to normal and the electrocardiographic alterations in T waves and P-R conduction should have become stabilized

4. Taran advocates prolonged *oxygen therapy* in acute rheumatic fever. There is no evidence, however, that this alters the course of the disease except in case of cardiac failure.

5. Recently cortisone and *ACTH* (adrenocorticotropic hormone) have been used in the treatment of the active stage of rheumatic fever. These substances quickly bring about disappearance of the evidences of the infection. During treatment with ACTH the temperature, the white blood cell count, and the sedimentation rate all fall, the number of circulating eosinophiles in the blood decreases. The heart rate slows and its size decreases. The joint symptoms and signs regress as do the evidences of myocardial and pericardial involvement. Electrocardiographic abnormalities—the T-wave and RS-T abnormalities and prolongation of the P-R time—regress (Fig. 36). The vital capacity increases. The patient feels better. Attacks of active rheumatic fever and rheumatic carditis have been promptly terminated in the early stages upon the administration of ACTH. In other cases the evidence of carditis may disappear more quickly, so that patients may become ambulatory within two to four weeks after the onset of the disease. It is apparently more effective in the exudative than in the proliferative stage of the disease. Fever and polyarthritis respond most rapidly, in 24 hours and in two to three days respectively. Acute pericarditis disappears within two to three days. Rheumatic nodules decrease in size in seven to ten days and disappear in six to seven weeks. In certain instances chorea has improved. Murmurs indicative of mitral and aortic valvular damage have disappeared during the course of ACTH therapy, but it is not to be expected that long-standing valvular deformity would disappear. If ACTH is given over a short period in moderate doses there need be no disturbance of electrolyte balance and no undue accumulation of fluid. Fluid should be restricted during this period and a low sodium diet used.

ACTH has been used with benefit in patients with active rheumatic fever and carditis with heart failure. There are two opposing effects of the drug In the first place ACTH may cause accumulation of fluid and aggravate the heart failure. On the other hand ACTH suppresses the active rheumatic inflammatory process and with improvement of myocardial function heart failure is relieved. The net result depends on which of them occurs first and more strongly. Heart failure may improve to the extent that mercurial diuretics can be discontinued

The use of this drug in this disease is in the investigative stage; dosage and duration of therapy are unsettled. In children its administration over a period of seven to eight days in decreasing dosage has been effective Doses of 80 mg. given intramuscularly in the first and second 24 hours, followed by 60 mg the next three days and 40 mg. on the next two days, may be adequate. The dosage might be 100, 80, and 60 mg respectively on the days indicated above in older children or in those of greater body weight, for whom the smaller amount appears inadequate. Adults may require still larger amounts Some observers advise smaller doses than those given above, and prescribe the drug over longer periods of time Others give the drug first in full suppressive doses, then in small maintenance doses until it is apparent that the acute rheumatic state has disappeared Variations in potency of different batches of ACTH may account for some of the differences in amounts of the drug which have been effective. In the treatment of rheumatic

PLEURITIS AND PNEUMONITIS. Removal of the fluid by chest tap may be necessary when pleuritis with pleural effusion occurs. Salicylates are usually effective. When there is chest pain codeine and strapping of the chest give relief. Pulmonary changes which have been designated as rheumatic pneumonitis have been described in the course of active rheumatic fever.

Treatment of Cardiac Manifestations

The treatment of the cardiac manifestations of acute rheumatic fever will be considered separately to treatment during rheumatic heart disease. The latter will be found on pp. 220–234.

MYOCARDIAL AND ENDOCARDIAL INVOLVEMENT. Salicylates appear to have no beneficial effect in the treatment of the myocardial or endocardial manifestations. The early exhibition of ACTH in some patients has rapidly terminated the signs and symptoms of myocardial involvement (p 214) and the murmurs resulting from endocardial involvement have disappeared The most important part of therapy is the immediate and prompt treatment of heart failure when it arises. Rest in bed is required until evidences of activity of the myocardial lesion have disappeared.

ACUTE PERICARDITIS AND PERICARDIAL EFFUSION. Sudden dyspnea, hacking cough, panting respirations, and precordial pain suggest the onset of acute pericarditis and carry serious prognosis. Auscultation should be made at frequent intervals in order to detect a pericardial friction rub Fullness of neck veins, increase in the area of cardiac dullness, and fall in blood pressure indicate the probable appearance of fluid in the pericardial cavity. Application of an ice-bag to the precordium and use of a sedative such as codeine may provide relief from pain Adequate doses of salicylates may lead to absorption of pericardial effusion.

If fluid accumulates rapidly and compression of the heart is extreme, pericardial tap may be necessary Fluid should be removed slowly in order to avoid sudden dilatation of the heart The needle is best inserted at the apex It is often difficult, especially in children, to differentiate fluid from a large dilated heart.

In the presence of pericarditis with effusion, digitalis is contraindicated, it reduces the size of the heart, and this does not appear wise since the organ is already compressed so that it cannot relax adequately in diastole to admit blood into its chambers. The provision of oxygen may be beneficial. Salicylates will not always prevent the occurrence of pericardial effusion It is unusual, however, for effusions of significant size to occur if the patient is on salicylate medication and other signs of the disease are adequately controlled The prompt use of ACTH in adequate dosage has brought about a rapid regression of the signs and symptoms of pericardial involvement (see p 214)

HEART FAILURE Heart failure in active rheumatic fever is usually due to myocardial involvement, namely, to active carditis It is not caused by valvular involvement unless the patient has had rheumatic fever previously and active carditis has been superimposed upon a valvular defect The onset of a recurrent attack of acute rheumatic fever may precipitate heart failure in a heart which otherwise was compensated until the active carditis was superimposed Practically 100 per cent of patients under 20 years of age and a high percentage of those under 30

before salicylate therapy is discontinued. The dosage of the drug is decreased over a week or ten days before the drug is withdrawn completely. Jones warns of too prolonged use of salicylates as this may mask symptoms and alter the course unfavorably but other investigators feel that this fear is not warranted.

Unless the disease is of the chronic type, the patient is kept in bed until all evidences of rheumatic activity have disappeared. The patient should be observed for one to two weeks without salicylates before mobilization is started, in order to see if there will be recurrence of symptoms or signs of active disease.

The mobilization of the patient after the acute phase is discussed on page 220.

Treatment of Specific Noncardiac Manifestations

CHOREA. Chorea is part of the tetrad: *tonsillitis, rheumatic fever, chorea,* and rheumatic heart disease. It is accepted as a manifestation of rheumatic fever by most investigators in this field. In about 25 per cent of rheumatic fever cases, it occurs without other evidence of the disease. It may accompany polyarthritis and carditis. It has been seen less frequently in the last twenty years but is still one of the most common manifestations of rheumatic fever. However, nowadays it is less severe and fatal cases are uncommon. The patient should be at complete rest in bed, alone in a room if possible. Phenobarbital or warm baths may have a soothing effect. The food intake should be high, with vitamin supplements for patients who have a prolonged course. On the other hand, a regimen of low food intake or a ketogenic diet for a few days has been found to decrease the choreiform movements temporarily. Fever therapy is too vigorous and is not generally advocated since it must be used with great care in order not to lead to harm. There are contradictory reports about the effectiveness of ACTH and cortisone (p. 214).

It must be kept in mind that chorea is a chronic manifestation of rheumatic activity, occurring most commonly in early adolescence. It may persist for many months and recur year after year during this period The prognosis is good

RHEUMATIC ENCEPHALITIS. Rheumatic encephalitis has been reported during active rheumatic infection. It is not alleviated by the use of salicylates, in fact, salicylate toxicity may conceal the symptoms of encephalitis The two can be distinguished by the fact that hyperventilation occurs in salicylate toxicity but not in rheumatic encephalitis

There may be hallucinations, phobias, acute episodes of panic reaction, delirium, restlessness, and convulsions. Hyperpyrexia may occur. Mental retardation, sleeplessness, and masklike facies may be the only symptoms. Some patients may have focal lesions suggesting the embolic phenomena of subacute bacterial endocarditis. Anesthesia may be required to control the maniacal state to prevent physical exhaustion and additional cardiac damage.

NODULES. The incidence of rheumatic nodules varies. The nodules are found along the tendon sheaths and in the scalp, and indicate a severe infection with poor prognosis. Salicylates have no effect ACTH has been thought to bring about regression of nodules in some patients This manifestation is not as rapidly influenced as the other rheumatic manifestations (p 214).

EPISTAXIS. The cause of epistaxis in active rheumatic fever is not known It is not due to the use of salicylates, and is treated in the appropriate manner.

CARDIAC IRREGULARITIES. Most of the known cardiac irregularities may occur in the active stage of rheumatic fever and are usually evidence of myocardial involvement. The most common are those relating to the conduction system, in which there may be all grades of block: prolongation of the P-R conduction time, block of occasional sinus impulses, high-grade block such as 2:1, and finally complete heart block (Fig 35) Changes in the conduction time are so frequent that they are accepted as evidence of rheumatic activity on appropriate occasions. Transient bundle branch block may occur (Chapter 5).

In addition to the conduction defects, transient auricular fibrillation, auricular flutter, auriculoventricular and auricular paroxysmal tachycardia, and, less rarely, ventricular paroxysmal tachycardia may occur Premature contractions may arise from the auricles, auriculoventricular conduction system, or the ventricles

The treatment of these irregularities in the active stage of rheumatic infection is essentially the same as in other circumstances. Frequently they are transient and require no special therapy Salicylates have no beneficial effect The treatment of cardiac irregularities during rheumatic heart disease is given on page 228

When *auricular fibrillation* occurs in the course of active rheumatic infection it is usually transient. If the patient exhibits no signs of heart failure and does not develop any within a few hours, and if the ventricular rate is not excessively rapid, careful supervision can be maintained without special therapy. If there has been evidence of active carditis and heart failure appears the patient should be promptly digitalized The urgency dictates whether a rapidly acting intravenous preparation or an oral preparation is to be chosen. It is necessary to observe special caution to prevent toxicity If auricular fibrillation persists after digitalization with adequate slowing of the ventricular rate, quinidine should be used provided there are no contraindications Auricular fibrillation should not be allowed to become chronic at this stage of the life history of the patient.

Auricular flutter may be transient and require no therapy but if it is persistent and signs of heart failure begin to appear, digitalization should be carried out as in patients with auricular fibrillation If adequate doses of digitalis do not bring reversion to normal rhythm quinidine should be used Auricular flutter is an ineffective rhythm and the longer it persists the more difficult it may be to cause reversion to normal sinus mechanism

In the case of paroxysmal tachycardias, if the patient's general condition is good and signs of heart failure do not appear, a few hours may be allowed for spontaneous reversion to normal rhythm If the tachycardia persists, reversion should be brought about by the usual measures, care being exercised when digitalis is used that toxicity does not occur.

Premature contractions are transient in active rheumatic fever and seldom require therapy They give evidence of myocardial irritability. Sedatives may be used when the contractions disturb the patient

Changes in conduction, including the high-grade and complete *heart blocks*, are usually transient and require no therapy I do not recall seeing syncope with the onset of complete heart block in active rheumatic carditis Should it occur, it is treated as other instances of Adams-Stokes syndrome due to complete heart block.

years of age dying of rheumatic heart disease have active carditis. In the later decades coronary artery disease impairs the myocardial capacity and may lead to heart *failure in the presence of valvular disease* The state of the myocardium is more important than the valve lesion. All the common manifestations of heart failure may be encountered.

Heart failure has been favorably influenced by the use of ACTH (p. 214).

In adults, heart failure in the presence of acute rheumatic fever receives the same treatment as failure resulting from other causes (see Chapters 1 and 2) *Digitalis* is used in the same amount and dosage. However, the drug should be given cautiously because these patients occasionally appear to develop an intolerance for digitalis and are prone to develop arrhythmias. Sudden death has been recorded Arrhythmias occur spontaneously as a manifestation of the acute rheumatic carditis, and it is not clearly demonstrated that digitalis contributes to their appearance. Nevertheless, premature contractions and other irregularities such as auricular fibrillation and defects in P-R conduction time should be watched for, before each dose. Blumgart was of the opinion that digitalis did not further prolong the P-R time even though it was already increased by the activity of the rheumatic fever. *Mercurial diuretics* should be used promptly at the first appearance of heart failure. I prefer to give these in the usual manner at two- to three-day intervals rather than daily. The xanthine diuretics, especially theobromine sodium salicylate, may be used (see Chapter 1). They are often very effective agents. With onset of heart failure it may be expedient to use acetylsalicylic acid without sodium bicarbonate because the sodium ion may lead to the retention of water. Oxygen may be required, especially if there is pericardial involvement. The fluid intake should be restricted to 1500 to 1800 cc., if fever makes it inadvisable to limit it further.

In children, Jones prefers to use xanthine and mercurial diuretics before digitalis. He thinks digitalis may improve one-third of the patients but may harm others. As noted above, arrhythmias may be induced by digitalis. He recommends the amount given should be in proportion to the adult on the basis of the body weight In my experience, children with rapid auricular fibrillation require approximately the same amount of digitalis to slow the ventricular rate as that required by an adult weighing several times as much The effect should be attained without nausea and vomiting. It may be that children who require digitalis are more seriously sick and have greater myocardial damage, so that arrhythmias are to be expected to occur more frequently even though digitalis were not given Jones thinks children gain little by salt restriction, he is of the opinion that glucose given intravenously may be useful in treating heart failure in these patients.

Children with chronic heart failure and low-grade chronic rheumatic activity may be kept on a limited ambulatory regimen similar to that adopted for some adult patients.

The functional state of the heart can be altered sharply by recurrence of the rheumatic infection or by the occurrence of a streptococcal infection; in either case failure may appear or, if already present, become worse. Patients may remain compensated as long as they are protected from streptococcal infections Every patient with rheumatic heart disease and rheumatic fever should be protected by isolation against streptococcal infections.

may cover a period of months to years. Each recurrence may increase the valvular damage or additional lesions may be superimposed Mitral involvement alone is the most common lesion; next, mitral and aortic combined, much less frequently, aortic alone, and less frequently still, tricuspid involvement. Smith and Levine, and Cooke and White have shown that the more carefully the signs of tricuspid stenosis are looked for on clinical examination, the more frequently this lesion will be found For example, in a patient with mitral stenosis, mitral insufficiency, aortic stenosis, and aortic insufficiency there is a fair chance that tricuspid stenosis and tricuspid insufficiency will also be present. The effect of ACTH on the incidence of valvular disease, if the drug turns out to be of use in the routine treatment of patients with active rheumatic fever, cannot now be predicted

The natural history of the disease in patients with each of these valve lesions differs; for instance, a patient may have mitral stenosis for many years without cardiac enlargement and remain without symptoms as long as he is free of active disease. A history of clinical rheumatic fever is elicited in only 50 per cent of patients with mitral stenosis. A patient with mitral stenosis will begin to have symptoms earlier than a patient with aortic insufficiency but responds satisfactorily to treatment and survives for many years On the other hand the patient with aortic insufficiency carries on for many years with no limitation of functional capacity and a large heart, but when this patient begins to have symptoms and heart failure ensues, the downhill course is more rapid and progressive Patients with tricuspid stenosis and insufficiency and mitral stenosis and insufficiency may do better after the onset of failure than patients with mitral stenosis and insufficiency without tricuspid stenosis. the stenosed tricuspid ring may prevent the delivery to the heart of more blood than the stenosed mitral opening can conduct through its orifice. Most of these patients have ascites and enlargement of the liver Levine is of the opinion that patients with mitral stenosis who also exhibit hypertension may carry on better than patients without hypertension, the hypertension presumably giving some dilatation of the mitral ring through left ventricular enlargement Stewart and his associates thought that aortic insufficiency in the presence of mitral stenosis may serve the same functional purpose

In the presence of mitral stenosis and insufficiency the cardiac output before the onset of heart failure may be diminished as compared with normal subjects (Stewart and associates) The addition of aortic insufficiency to mitral stenosis and insufficiency usually makes the restriction of cardiac output less marked. The combination of mitral stenosis and insufficiency with aortic stenosis and insufficiency causes the greatest reduction of cardiac output.

Interest has been exhibited in the association of rheumatic fever and *rheumatoid arthritis* Patients may have attacks of definite acute rheumatic fever in early life associated with typical rheumatic valvular disease and later exhibit evidence of typical rheumatoid arthritis There are other instances in which the patient with rheumatoid arthritis has clinical evidence of valvular disease without giving a history of preceding overt rheumatic fever. Finally there are patients who have rheumatoid arthritis without clinical evidence of valvular involvement, who show valvular involvement at autopsy The reported incidence of such a combination ranges from 5 per cent up to approximately 40 per cent.

Mobilization After Rheumatic Fever

Patients with prolonged, chronic active disease may be allowed limited activity rather than being kept at rest in bed. This applies especially to children with low-grade prolonged rheumatic infection. There is little evidence that the course of the rheumatic activity is altered by moderate activity. While rest may not control the disease or the development of valvular heart disease it may alter the functional capacity of the heart. There are no data available on this point. This program takes into account the psychic trauma of prolonged bed rest and inactivity in young children If, however, acute carditis is present with failure, complete rest in bed must be enforced.

PATIENTS WITHOUT CARDIAC SEQUELAE. The patient should remain in bed two weeks after the disappearance of all signs of activity and after salicylates have been discontinued. Mobilization is then undertaken gradually. The patient sits on the side of the bed on the first day, then sits in a chair one-half hour the next day, followed by one-half hour in the morning and in the afternoon the next. On successive days the time spent sitting up is then increased by a quarter of an hour in the morning and afternoon, until the time sitting up in the chair has reached five to six hours daily The patient then begins walking while the six-hour sitting up period is kept constant After this, lavatory privileges are allowed. Finally a tub bath is permitted. Approximately two weeks are required for the patient to get back to taking care of himself, and return to normal activity is then gradually undertaken. A patient who has recovered from rheumatic fever without cardiac involvement is permitted to lead a normal life. The plan of mobilization may be shortened in patients in whom the course of rheumatic infection has been abbreviated by the use of ACTH.

PATIENTS WITH CARDIAC SEQUELAE. If the patient has suffered cardiac sequelae such as valvular disease during this episode of active rheumatic fever or previously, and has chronic valvular disease, mobilization is undertaken in the same manner as above, except that it is instituted somewhat more slowly. How much physical activity is finally achieved depends for the most part on the status of the heart.

RHEUMATIC HEART DISEASE

Natural History as a Background for Management of Rheumatic Heart Disease

The following brief summary is necessary to give a background for the management of a patient who has had rheumatic fever. The patient may have rheumatic involvement of the various parts of the heart and recover without any evident cardiac damage Commonly there is valvular damage and less commonly adhesive pericarditis. The more frequent the recurrences, the more likely the patient is to develop permanent cardiac damage, and the greater the cardiac damage to be expected. Also, the earlier in life the first attack occurs the more likely the patient is to have recurrences Such patients should be given prophylactic therapy (see page 222). Adolescents are prone to have recurrences.

From the occurrence of infection to the establishment of valvular heart disease

New York. This procedure is obviously applicable to only a small number of patients It is seldom satisfactory to send patients to Florida or southern California for this purpose because the constant flow of the population back and forth from the North seeds these southern areas with streptococcal infections.

Drugs

SULFADIAZINE. The use of a daily ration of sulfadiazine 0 5 Gm twice a day has been found to reduce the number of recurrences of active rheumatic fever In young individuals 0.5 Gm. of the drug daily may be adequate The blood level of the drug runs from 1.5 to 3 5 mg per 100 cc. on this regimen The patient should drink at least two quarts of water daily The use of sodium bicarbonate is not necessary on this dosage. Kidney damage has not resulted from this regimen

The patient should be kept under close supervision and the blood levels of the drug and white blood cell count taken at regular intervals Sulfadiazine should be discontinued if the white blood cell count falls. The experience of Thomas and others over several years indicates that the drug can be given without ill effects if the patient is observed carefully. The patient should be followed closely for the first six weeks of the sulfadiazine regimen, then at intervals of one month, three months, and six months If no untoward reaction occurs during this time the follow-ups can then be continued at further six-month intervals.

While the use of ration doses of sulfonamide drugs prevents the occurrence of streptococcal infections and the incidence of rheumatic fever, there is some evidence that they are ineffective when used after the development of streptococcal infection.

SALICYLATES. The use of a daily ration of sodium salicylate 4 0 to 6 0 Gm a day has not been convincing enough to put to general use It has the disadvantage that it may mask symptoms of activity

PENICILLIN. Ration doses of penicillin have been found to reduce the incidence of respiratory infections and recurrence of rheumatic infections Its effects over long periods of time are being studied There is no good evidence that the use of inadequate doses leads to the appearance of resistant strains of beta hemolytic streptococci Goerner, Massel, and Jones report that the use of penicillin for ten days to eliminate beta hemolytic streptococci from the throats of patients in close contact with persons who have had rheumatic fever is a practical way of protecting the latter from infection due to this group of organisms

Denny, Wannamaker, Brink, Rammelkamp, and Custer have presented evidence that rheumatic fever can be prevented by the treatment of streptococcal disease with penicillin. In only 2 of 798 patients with streptococcal infections who were treated with penicillin did acute rheumatic fever subsequently develop On the other hand in a parallel control group of 804 untreated patients, 17 developed rheumatic fever Suppression of antistreptolysin-O response and eradication of the streptococci occurred in many patients Streptococcal infections must be diagnosed and treated early if the incidence of rheumatic fever is to be reduced materially by the use of penicillin The dosage they found effective was 300,000 units as the initial dose, repeated in 48 hours, and followed by 600,000 units 48 hours later.

Kohn, Milzer, and MacLean found that the recurrence rate of rheumatic fever

The electrocardiogram may be normal except for low amplitude of the QRS complexes. The heart is large by x-ray examination in about 25 per cent of the cases. There are several points of view: that the two diseases are the same with different constellations of manifestations, that the two diseases are different responses to the same etiologic agent; and finally that they are two different diseases. In a patient who has had rheumatic fever with valvular disease, and has rheumatoid arthritis as well, it might not be possible to decide, upon recurrence, whether there is renewed activity of rheumatic fever or of rheumatoid arthritis. Sedimentation rate, skin rashes, and nodules may not be differential points as they occur in both. Even though there may be cardiac involvement in rheumatoid arthritis, heart failure is not common in these patients. Moreover patients with typical rheumatic valvular disease who later have rheumatoid arthritis suffer less functional impairment of the cardiac capacity with a later incidence of heart failure, probably *because the rheumatoid arthritis limits the activity which can be undertaken.*

Prevention of Recurrences of Rheumatic Infection

Patients with rheumatic heart disease may carry on satisfactorily until a streptococcal infection precipitates another episode of rheumatic activity or until an intercurrent infection places an additional burden on the heart. Attacks of acute bronchitis, upper respiratory infections, and pneumonia are especially likely to increase the load and lead to heart failure. In other instances the onset of Graves' disease may be the factor which increases the demands on the heart.

The prevention of rheumatic fever is difficult because the exact etiologic cause is unknown. Although beta hemolytic streptococcal infections initiate the disease, the susceptible individual cannot be distinguished from the nonsusceptible. No prophylactic measures are available for use in the general population except those of general hygiene, avoidance of overcrowding, and care of colds and respiratory infections.

Epidemics of rheumatic fever have been reported. In such groups sulfadiazine or penicillin may be given to the exposed individuals. All the reported epidemics were preceded by beta hemolytic streptococcal infections. The use of sulfadiazine 0.5 Gm. twice a day is definitely effective as a prophylactic agent to prevent recurrence of rheumatic infection. More recently ration doses of oral penicillin have also prevented recurrences of rheumatic fever.

General Recommendations

The patient should be told how to live: long hours of sleep, nutritious food, avoidance of overexcesses, avoidance of exposure to bad weather, avoidance of overheating or chilling, avoidance of swimming in cold water are a few of the recommendations. Every respiratory infection should be treated with care, the patient remaining home in bed during its height. Careful observation for signs of rheumatic fever should be made in the period afterward.

CHANGE IN ENVIRONMENT. It has been found that patients subject to recurrences of rheumatic infection remained free of them in a climate similar to Puerto Rico. This benefit is due to the fact that fewer streptococcal infections occur in the tropics. Recurrences of infection were observed when patients moved back to

Adults

When it is discovered that an adult has rheumatic heart disease the patient should be shown gradually all that this means for him The usual pattern of activity is analyzed in order to adapt it most beneficially. It is not enough to tell the patient "not to do too much" I recommend that patients always stay below what they are able to do comfortably. They should do everything slowly The following points are emphasized: not to walk stairs when elevators are available; when stairs are required, to climb them slowly, resting every few steps and on landings; to go slowly on hills, to bathe in warm water (swimming in quiet water may be allowed, but the patients should never get into situations in which they have to push themselves and cannot stop swimming when they wish), to avoid exposure to colds and respiratory infections (see p. 226). In combating a cold the patient should remain at home in bed a day or so, and be alert for recurrence of rheumatic infection ten days to three weeks afterward Adequate sleep should be secured Excesses of alcohol and smoking should be avoided. Regular vacations should be required. The physician should help the patient to select a job which is compatible with his functional capacity. The patient can be trained to try to prevent the onset of failure without a morbid interest in his disease The physician should be consulted about the advisability of marriage and its obligations: increase in the effort to make a living, and the advisability of pregnancy It is kept in mind that most adults in order to earn a living have to do enough walking in carrying out their daily activity to make it unnecessary to undertake regular exercise. If there is a tendency to gain weight it may be prevented by restriction of the caloric intake

Occasionally an adult patient with rheumatic heart disease who has had attacks of heart failure but is well controlled on a regimen becomes dissatisfied with limitations and decides to stop taking medicine and to give up restrictions, with the idea of having a "short life" and "going at a rapid pace to the end" When cardiac failure recurs with its discomforts they usually see the folly of this course and eagerly consent to return to the regimen. Sometimes these episodes of rebellion can be seen in the making. Encouragement and discussion of the problems with the patient may forestall their occurrence Patients must be given constant support and encouraged to live at peace with the restrictions which are necessary.

Treatment of Patients with Inactive Rheumatic Heart Disease During Failure

The [illegible]
does r[illegible]
types [illegible]
go on for a long time before there is a recurrence if adequate care is provided and suitable precautions are taken In other instances, however, the number of recurrences builds up in a crescendo until there is chronic heart failure (p. 226). Patients should be taught to avoid the things which are likely to precipitate failure.

The measures which are of most help in the treatment of heart failure are

was zero in a penicillin-treated group compared with 11 and 19 per cent in two control groups they studied. The schedule of oral administration of penicillin which they found effective was 800,000 units daily for seven consecutive days for the first week of each month throughout the school year. This regimen significantly reduced the incidence of hemolytic streptococcal infections in the throats of children who had had rheumatic fever. According to the available data, this regimen would be repeated each year.

RHEUMATIC HEART DISEASE AND HEART FAILURE

Care of Patients Before Occurrence of Failure

In my experience patients with rheumatic heart disease do best in the long run under a regimen of limited activities even though they have no symptoms. Each case must be individualized.

Children

The emotional trauma of a crippling disease such as rheumatic fever early in life has to be kept constantly in mind These young persons have illnesses which require long periods of complete rest in bed and separation from playmates. When they are again permitted to go to school modifications in schedules may be necessary which set them apart from other children. Most children weather these stresses and grow into stable adults Some children learn early to use their illnesses to gain their own ends Others become defiant at restraint and cannot be persuaded to accept any restrictions In fact, in the adolescent stage they may become resentful and engage in excess activities

When children become old enough to discuss their disease and its handicaps the problems become less difficult. The attempt is made to have the child see that childhood and adolescence are transient phases on the way to adulthood, that playing strenously is of importance for only a few years, and that the main objective is the business of growing up, of acquiring as much education as possible with the capacity to earn a living as early as possible during adult life. The child should be encouraged to talk about his ambitions and aims. These expressions may be gradually modified until they become realistic

In a school child the physician has to know how the patient gets to school; how many flights of stairs he must climb; whether the gymnasium course can be adapted to the patient's functional capacity; what the patient will be expected to do at play. These questions should be discussed with the child, the teacher, and the parents. Care should be exercised not to make the child or the parents overanxious. It is not uncommon for children with rheumatic heart disease to suffer from many of the symptoms of neurocirculatory asthenia. None of these will be related to the cardiac disease per se but are caused by anxiety about the heart or by having been told inexpertly about the presence of a murmur. A child can be told cautiously that he has heart disease in terms which can be understood and without giving rise to apprehension In many, a normal life may be possible with the exclusion of competitive sports.

acute tonsillitis or of respiratory infection symptomatic treatment is employed: hot gargles, aspirin, and codeine may give relief.

Patients with rheumatic heart disease are especially subject to attacks of acute *bronchitis* The harm which this intercurrent infection can cause is underestimated It may induce heart failure. The discovery of râles in the chest is frequently mistaken for diffuse bronchopneumonia instead of acute bronchitis. The prompt use of oxygen may lessen the load on the heart in these patients. Aminophyllin 0.24 to 0.48 Gm. may be given intravenously several times a day. Steam inhalations with tincture of benzoin every four hours for 20 minutes may lessen the wheezing and loosen the secretions. It may be wise to use penicillin if there is no evidence of active rheumatic infection.

An acute infection may precipitate heart failure in a patient with rheumatic heart disease who has never had failure or who usually maintains compensation with adherence to a regimen. In the presence of acute infection it is my practice to keep the daily fluid intake to around 1500 cc. in patients who have had failure and are on a "cardiac regimen" even though there is fever. The amount may be increased to 1800 cc. daily if there is sweating and if the patient suffers an illness associated with rise in temperature. Mercurial diuretics, salt-poor diet, and digitalis should be continued I have seen many patients go into heart failure during attacks of acute bronchitis or respiratory infections when fluids were forced too vigorously. I have seen only benefit from restricting fluids in these patients Should occasion arise requiring sulfadiazine the urine should be examined frequently for sulfa crystals and for red blood cells Sodium bicarbonate should not be used to cover sulfadiazine if the patient has had failure. Potassium bicarbonate should not be used as a substitute for the sodium salt; cardiac poisoning with auricular standstill has been recorded following its use for this purpose (Fig 64).

When cardiac patients suffer pneumonia the precautions given in the paragraph above apply with respect to fluid intake and drugs.

If a patient develops heart failure as a result of an acute infection, it is treated as are other instances of heart failure, the patient being kept in bed until free of failure, followed by gradual mobilization. A decision must be made whether the failure is due to the recurrence of active rheumatic fever or to the superimposition of infection upon the valvular disease

PREGNANCY AND RHEUMATIC HEART DISEASE

This subject is discussed fully in Chapter 28, in which a special section is devoted to rheumatic heart disease.

TREATMENT OF COMPLICATIONS AND CONSEQUENCES OF RHEUMATIC HEART DISEASE

The implications and treatment of cardiac irregularities in rheumatic heart disease are sufficiently distinct from those applying to the acute phase to merit separate discussion. The acute phase of the disease is considered on p. 219.

rest in bed, limitation of fluid intake, restriction of salt intake, full digitalization with continuance of maintenance amounts, mercurial diuretics, ammonium chloride, and oxygen The details are given in Chapter 1.

Treatment of Chronic Heart Failure in Patients with Rheumatic Heart Disease

Frequently patients will remain free of heart failure by the measures already described. Bouts of failure may be brought on by increase in physical activity or stress, respiratory infections, and recurrence of active rheumatic infection. These will respond to rest in bed and to the use of additional measures of therapy.

Many patients become uncooperative at one time or another. Other patients may find it impossible to restrict their activity sufficiently to keep them free of failure. Consequently they show varying degrees of heart failure all the time. It is not economically practical to keep most of these patients in bed for long enough periods of time, nor are the gains resulting from making them complete invalids sufficient to insist upon this plan. Patients may be unable or unwilling to cope with the salt-poor diet and low fluid intake. These patients may be kept ambulatory for many years by the use of mercurial diuretics every third day together with ammonium chloride, as well as with digitalis and by other measures. They may be unable to work, or may be able to do light housework in the home There evolves, however, a gradual increase in the signs of failure until it is again necessary to put the patient at complete rest in bed in a hospital or at home and, by rigid supervision, to restore compensation In stubborn instances removal of ascites or pleural effusions by paracenteses may be required.

Ambulatory Treatment of Heart Failure

When patients cannot be hospitalized or cannot remain in bed certain adjustments in the optimal regimen must be made The patient may be supervised first at home and with improvement come to the physician's office or to the clinic The diet and fluid regimen can be arranged, and digitalization as an ambulatory patient can be carried out as described in Chapter 3 (p. 95) Certain patients may be taught the self-injection of thiomerin subcutaneously (p. 40).

CARE OF ACUTE RESPIRATORY INFECTIONS IN PATIENTS WITH RHEUMATIC HEART DISEASE

Advice about the care of acute respiratory infections should be given to patients who have had acute rheumatic fever, whether or not they have rheumatic heart disease. They should be advised to avoid exposure to respiratory infections. If exposure occurs, 0 5 Gm. of sulfadiazine may be taken once or twice daily for several days. They should see their physician should they develop an acute respiratory infection. They should be advised to remain at home in bed for a few days when there is acute tonsillitis or acute upper respiratory infection whether there is fever or not. If streptococci are implicated, sulfadiazine or penicillin should be used. These patients should be on the alert for manifestations indicating recurrence of rheumatic infection ten days to three weeks later During the period of

and short runs of ventricular paroxysmal tachycardia may appear. At this stage of the disease the physician has to be content with giving the maximal amount of digitalis that the patient can tolerate as the maintenance dose with exhibition of the minimal degrees of toxicity. The treatment of premature contractions has been recorded in Chapter 5.

Embolic Phenomena

Mural thrombi may form in the hearts of patients with mitral stenosis especially during auricular fibrillation. Portions of these on becoming dislodged give rise to emboli Infarction of brain, kidneys, and spleen may occur, or closure of arteries supplying the legs and mesentery may take place when emboli arise from the left heart If emboli arise from the right heart pulmonary infarction may occur. Paradoxical embolization may occur if there is a communication between the two sides of the heart because of a congenital defect. Maintenance amounts of dicumarol or of heparin to patients with auricular fibrillation who exhibit embolic phenomena may prevent further episodes Attempts have been made recently to prevent arterial embolization from mural thrombi in mitral stenosis and auricular fibrillation by surgical removal of the left auricular appendage

Syncope

Patients with aortic stenosis may be subject to fainting attacks These may be associated with exertion. The mechanism of syncope in these patients is not known. Patients should avoid events which have been known to cause the attacks and should not carry heavy bags, run, or engage in strenuous prolonged exertion.

Subacute Bacterial Endocarditis

Subacute bacterial endocarditis was formerly the most dreaded complication of rheumatic heart disease It occurs in approximately 4 per cent of the cases It is uncommon after the onset of auricular fibrillation or of failure It is implanted most frequently on the mitral and aortic valves. Since the institution of penicillin therapy recovery is recorded in 75 to 80 per cent. After recovery the patient still has rheumatic heart disease and may also have more scarring and deformity of the valves Patients who have rheumatic heart disease or who have had rheumatic fever should observe good oral hygiene. Penicillin prophylaxis should be used if the extraction of teeth is undertaken Penicillin should be given in the treatment of acute tonsillitis, of respiratory infections, and prophylactically preceding and after childbirth Subacute bacterial endocarditis is discussed further in Chapter 22.

Hemoptysis

Hemoptysis is one of the most common accidents which patients with mitral stenosis suffer. Pulmonary hemorrhages occur because of increase in pressure in the pulmonary circuit due to obstruction by the narrow mitral ring. Hemoptysis is also common in patients with active rheumatic infection. Patients may exhibit hemoptysis as the sole manifestation of heart failure for many years. They may expectorate only small amounts of blood or of blood-streaked sputum, or may have profuse hemorrhages This must be differentiated from pulmonary infarction

HEART FAILURE

The treatment of heart failure has already been mentioned, and a more detailed account is given in Chapter 1.

AURICULAR FIBRILLATION

This is common in patients with mitral stenosis and less common in those with pure aortic involvement. Auricular fibrillation may precipitate heart failure but is not itself of ill omen. It is, however, a late complication of rheumatic heart disease. Two and one-half years is the average life span after the onset of auricular fibrillation but many patients survive its onset for many years. It may be paroxysmal or permanent. The treatment is considered in Chapter 5, p. 142.

Embolic phenomena occur in patients with mitral stenosis and auricular fibrillation. Most physicians hesitate to attempt reversion of the cardiac mechanism to normal rhythm with quinidine if auricular fibrillation is of long duration, if the heart is large, and especially if the patients have had heart failure. In such circumstances there is the possibility of precipitating embolization when reversion to normal rhythm occurs and the auricles begin to contract regularly and forcibly The prophylactic use of anticoagulants before, during, and after the use of quinidine may lessen this hazard That some patients feel better during auricular fibrillation and that the heart rate can be more satisfactorily controlled with digitalis during this rhythm than when normal rhythm is present must be taken into account before reversion is attempted

AURICULAR FLUTTER

Auricular flutter occurs as a paroxysmal rhythm, but may become permanent if not terminated by proper medication (see Chapter 5, p. 153). As it is an inefficient rhythm it may precipitate heart failure.

PAROXYSMAL TACHYCARDIAS

Auricular and nodal paroxysmal tachycardia and less commonly ventricular *paroxysmal tachycardia may occur in chronic rheumatic heart disease.* Their onset or persistence may precipitate heart failure They also occur in the course of active rheumatic fever. The treatment has been described in Chapter 5.

PREMATURE CONTRACTIONS

Premature contractions may occur without symptoms. They are common during heart failure and toward the end of the natural history of rheumatic heart disease but they also occur during active rheumatic infection. Ventricular premature contractions may occur as a sign of digitalis intoxication Auricular premature contractions may precede the onset of auricular fibrillation or auricular paroxysmal tachycardia As the heart size increases and the patient approaches the end of the life span, ventricular premature contractions may appear The irritability of the heart muscle increases The administration of sufficient digitalis to control heart failure induces ventricular premature contractions which may be frequent and give rise to coupling; on other occasions multiple ventricular premature contractions

Recurrence of Acute Rheumatic Fever

Recurrence of acute rheumatic fever is treated in the manner already described earlier. Constant forethought should be given to the prevention of recurrences (pp. 222–224).

Surgical Treatment of Mitral Stenosis and Other Valvular Defects

The possibility of surgical enlargement of the stenosed mitral valve was suggested by Brunton in 1902, and attempted by Cutler and Levine in 1923 For this purpose they devised a *valvulotome*, but the mortality from these attempts was discouraging Recently, with the wide attention given to the surgical treatment of congenital heart defects, and with increased experience in the treatment of these abnormalities, interest has again turned to the surgical treatment of mitral stenosis. Mitral insufficiency may be induced by enlargement of the mitral orifice. It is a question in each case whether the heart can sustain the degree of insufficiency which may be suddenly created.

Harken, Ellis, Ware, and Norman have recently subjected patients with mitral stenosis to certain corrective procedures In one group with a low resting cardiac output which could not be augmented by exercise, and with increased pulmonary artery pressure, they have performed *valvuloplasty*, in order to relieve the obstruction, using a cardiovalvulotome to enlarge the mitral opening In another group of patients with normal cardiac output which increased with exercise, increase in pulmonary artery pressure, but an indicated preponderance of mitral insufficiency, these investigators have made intra-atrial communications to decompress the left auricle In a third group of patients with mitral stenosis who had attacks of pulmonary edema with rapid heart action which was not controlled by medical means they performed in two stages bilateral upper thoracic sympathetic ganglionectomy, removing the inferior cervical ganglion and the first four or five dorsal sympathetic ganglia through a cervical incision During the surgical manipulation of the heart they gave procaine intravenously to reduce myocardial irritability.

Bailey and his associates have attempted to overcome the defect in mitral stenosis by *incision of the valve commissures*, dividing the scar tissue down to normal valvular tissue They think that the remaining normal valvular tissue then acts like a hinge, so that the cusps freely separate and approximate. They have devised a knife that fits on the exploring finger, which is inserted in an opening in the left atrial appendage By making the incision at the commissures the creation of a significant degree of mitral insufficiency is avoided. In most patients *manual dilatation* of the mitral orifice has been carried out. For patients with systemic embolic phenomena valvulotomy may be combined with left auricular appendectomy

Bailey has operated on 150 patients with mitral stenosis, with a mortality rate of around 10 per cent Disappearance of presenting symptoms, decline in pulmonary arterial pressure, and reduction in left auricular and over-all heart size have characterized the favorable responses. Seventy-five per cent were improved, many to the point of clinical cure. Bailey tries now to make an adequate opening, having been content at first with moderate improvement The criteria for the selection of patients for operation have not been sharply defined, since the procedure is in the

especially if the administration of anticoagulants is contemplated. These drugs are of course contraindicated in the presence of hemoptysis due to mitral stenosis. Many of the patients exhibiting hemoptysis are erroneously thought to have pulmonary tuberculosis and are sent to pulmonary and tuberculosis clinics.

When pulmonary hemorrhages occur patients should be put at complete rest in bed and given morphine, digitalis, mercurial diuretics, and oxygen. Penicillin may prevent infection should blood drain into the pulmonary tree. Although the hemorrhages may be large and cause the patient apprehension, bleeding usually stops before the loss of blood is serious. They should remain in bed until all trace of blood has disappeared from the sputum and compensation has been restored. Mobilization should be gradually instituted when recovery has been attained.

Ball Thrombus

A ball thrombus in the left auricle may form in the presence of rheumatic heart disease with mitral stenosis and auricular fibrillation. The thrombus may be the cause of attacks of syncope if it obstructs the flow of blood from the left auricle to the left ventricle. Obstruction is more likely to occur when the patient is sitting or standing than when he is recumbent. Death may result if the thrombus becomes wedged in the stenosed mitral orifice. One instance of ball thrombus in the right auricle has been reported in a patient with mitral stenosis and auricular fibrillation. This patient had attacks of acute air hunger and of marked cyanosis. Because of the great strides which have been made in cardiac surgery, it might be possible to evacuate the ball thrombus by opening the auricular appendage if the diagnosis can be made with a reasonable degree of accuracy.

Tonsillectomy and Tooth Extractions

Penicillin should be given for 24 hours before tonsillectomy and dental extractions or manipulation and for 48 hours afterward, as a prophylaxis against subacute bacterial endocarditis. Procaine penicillin might be given intramuscularly in 200,000-unit amounts two to three times a day or as 50,000 units of the aqueous solution every two to three hours for 24 hours beforehand and 48 hours afterward. Other investigators give the first dose four to six hours before extraction and a large dose just before extraction, and continue adequate doses for two days afterward. Sulfadiazine 1.0 Gm. together with sodium bicarbonate 1.0 Gm. every four hours may be used for this purpose if penicillin is not available but may not afford adequate protection. Aureomycin has also been used before dental extractions (p. 447). The state of compensation of the patient should be watched carefully during and after these operative procedures.

Tonsillectomy is not now so enthusiastically advocated in patients with acute rheumatic fever and rheumatic heart disease as it formerly was. Available statistics do not indicate that recurrence of rheumatic fever is prevented by this procedure. The same indications exist for tonsillectomy and adenoidectomy in rheumatic fever patients as in normal subjects. If tonsillectomy is indicated, it should not be done until after recovery from acute rheumatic fever. It is better done when the patient is in good condition after a short holiday and should be followed by an adequate period of convalescence. Elective tonsillectomy should not be done during the poliomyelitis season.

by Gibbon and his associates. In animals they have been able to reconstruct cardiac valves from venous and pericardial grafts. If their system or some other system for the maintenance of an extracorporeal circulation is perfected for use in human beings, operations upon the human heart under direct vision will be possible Lesions which are now inaccessible will be susceptible to repair. Moreover the possibility of providing rest for the heart in acute cardiac failure or following myocardial infarction by maintaining circulation with the pump-aeration system may point the way to new means of therapy in these difficult situations.

These surgical procedures—which are still in the experimental stage—have been briefly mentioned to indicate the trends at the present time. We can be encouraged to think that means will be found to overcome many of our present difficulties in operating on an organ which must continue to maintain an adequate circulation during the manipulation

Adhesive Pericarditis

The pathologic physiology in pericarditis with external adhesions is different from that prevailing in chronic constrictive pericarditis (Chapter 21). In the latter the thick, fibrous, perhaps calcified pericardium constricts or compresses the heart and interferes with its filling in diastole and with its contraction in systole. So far as is known rheumatic infection has not been implicated in this syndrome On the other hand the most common cause of adhesive pericarditis or mediastino-adhesive pericarditis is rheumatic fever Valvular defects are also commonly present. Consequently the heart is large, and constriction does not occur. In this condition with each cardiac systole the heart has to contract against and pull in the chest wall and the unyielding bony cage of the chest The work which the heart must do is thereby increased, although its volume output is seriously compromised It is in this syndrome that *Broadbent's sign* is seen

In patients with adhesive pericarditis *cardiolysis* (Brauer) may be of benefit This operation can be carried out under local anesthesia even in very sick patients A curved C-shaped skin incision is made over the left fifth rib anteriorly and the skin and subcutaneous tissue reflected to expose the third, fourth, fifth, and perhaps sixth ribs from their attachments to the sternum laterally for 8 to 12 cm on the left By blunt dissection several centimeters of these ribs are removed together with the periosteum, to prevent regeneration of the ribs The intercostal structures are removed by sharp and blunt dissection. Care is exercised to avoid entering the pleural cavity. Should this occur the usual measures are taken

With removal of the ribs the heart is seen to be covered with a soft, yielding tissue which retracts easily during systole A part of the sternum may be removed with rongeurs if the heart appears to be adherent to it The subcutaneous tissue and skin are brought together to cover the heart Recovery should be prompt

This operation has been carried out in only one of our patients She was a woman 40 years of age suffering from mitral stenosis and insufficiency, and aortic insufficiency of rheumatic origin Chronic auricular fibrillation was present Chronic congestive heart failure had been manifest for several years Mercurial injections had become less and less effective. Hospital admissions occurred at an accelerated pace because of recurrent ascites and exacerbation of congestive phenomena. Because of the clinical evidence of mediastino-pericardial adhesions the

experimental stage. Patients who have mitral stenosis with minimal insufficiency and without involvement of other valves are most likely to benefit.

At the New York Hospital Dr. Frank Glenn has operated for us on patients with predominating mitral stenosis and minimal mitral insufficiency. Manual dilatation has been the procedure used in most instances. Preoperative catheterization studies have given data about resting cardiac output, pulmonary pressure, shape of the pressure curves with respect to mitral insufficiency and tricuspid disease, and the response to mild exercise. We have accepted those with auricular fibrillation as well as those with normal rhythm; those with cardiac enlargement (roentgenograms, fluoroscopy, electrocardiograms) if it did not point to mitral insufficiency and aortic lesions, those with histories of hemoptysis, indicating increase in pulmonary pressure which might be reduced by enlarging the mitral orifice, those with histories of pulmonary infarctions; those with histories of pulmonary edema; those with chronic congestive heart failure who were unresponsive to medical therapy; and those without evidence of organic tricuspid disease, of active rheumatic infection, and of subacute bacterial endocarditis. Age has not been a deterrent factor. Long-term follow-ups of operated patients will reveal whether improvement which has resulted is maintained or whether the cut or fractured valves will seal together again.

Manual dilatation or commissurotomy of the mitral orifice has been done in a few patients who also have aortic insufficiency and/or stenosis. The extension of the operation to patients with these additional defects must be undertaken with caution.

Bailey and his associates have reported upon surgical attempts to correct mitral regurgitation, either by purse-stringing the valvular orifice using a pedicle graft of a strip of pericardium or using a piece of fascia lata

A few attempts have been made to enlarge the stenosed aortic valve Manual dilatation has resulted in fatality. On the other hand Bailey and his associates have successfully enlarged the aortic orifice in 2 patients using a dilating instrument inserted through the right common carotid artery.

Digital enlargement of the stenosed tricuspid valve has been attempted.

Bland and his associates have devised an operative procedure for the relief of recurring pulmonary edema secondary to advanced mitral stenosis. It is an extracardiac shunt to reduce the high pressure in the left auricle—pulmonary vein area by a communication with the systemic venous bed This is accomplished by the anastomosis of the dorsal segment branch of the right inferior pulmonary vein to the azygos vein. The volume of blood taking this circuit by-passes the stenosed mitral orifice. This procedure is rarely used at present because the communication may not remain patent.

Cossio and Perianes have carried out two surgical procedures with apparent benefit to patients suffering from permanent orthopnea and uncontrollable heart failure. In the first, tricuspid insufficiency was induced by inserting a valvulotome through the internal jugular vein into the right heart and cutting the valve. The rationale of this procedure was the clinical experience that tricuspid lesions frequently appeared to exert a beneficial effect in patients with mitral stenosis. In the second procedure they ligated the inferior vena cava below the renal veins

Of great importance for the future of cardiac surgery are the studies being made

SUMMARY

The cardiac sequelae of rheumatic fever rightly give cause for concern in its active stages since this infection is the major cause of heart disease in the younger age groups Until the etiology of rheumatic fever is known we are not likely to be able to cure or eradicate the disease. However, the present status of therapy in rheumatic fever shows certain advances which are reasons for a degree of satisfaction.

1. *Ration* doses of sulfadiazine may prevent streptococcal infections and thereby prevent recurrences of rheumatic fever in patients with or without rheumatic heart disease. Whether this will lower the later incidence of valvular disease in the absence of overt clinically rheumatic fever can only be learned after prolonged follow-up of these patients.

2. Ration doses of penicillin also prevent streptococcal infections and recurrence of rheumatic activity in the same patients Early treatment of streptococcal infections with penicillin will prevent the occurrence of acute rheumatic fever It is possible that the administration of large oral doses of penicillin daily for a part of each month of the school year will prevent recurrence of rheumatic infection in children

3 The abrupt termination of attacks of active rheumatic fever with carditis on the exhibition of appropriate amounts of ACTH in early and suitable cases is one of the most dramatic and encouraging trends in the treatment of rheumatic fever. Its use, however, is still in the experimental stage.

4 With the more accurate diagnosis of rheumatic valvular disease and closer supervision to insure that these patients live within their functional capacity, a longer interval may elapse before the onset of heart failure.

5. The newer mercurial diuretics represent great advances in the treatment of failure in rheumatic heart disease. On the whole, heart failure is now more effectively treated than was formerly the case. Patients may be kept free of failure for many years by a skillful use of the measures which are available, and may continue to lead active, economically useful lives When this is no longer possible because of the decline in functional capacity of the heart, patients carry on more comfortably on their restricted regimens for longer years than used to be expected.

6 One of the most feared complications of rheumatic heart disease, *subacute bacterial endocarditis*, can now be cured by the use of penicillin or other antimicrobial agents in 75–80 per cent of cases. Prevention of subacute bacterial endocarditis can be achieved by the prophylactic use of penicillin before dental extractions and tonsillectomy, and at other times when patients are susceptible to this complication.

7. The interest in cardiac surgery has spread from congenital malformations to acquired valvular disease. Enlargement of stenosed valve openings surgically by valvulotomy or by manual dilatation of the ring and the adaptation of certain palliative surgical operations in the management of patients with stubborn chronic heart failure due to valvular disease have proved effective with certain patients.

These gains in the treatment of rheumatic fever and its consequences are im-

operation was carried out by Dr. William D. Andrus after the functional capacity of the heart had become so seriously compromised that she had been hospitalized for many weeks. Removal of fluid from the abdominal and pleural cavities was carried out before operation to afford the patient maximal pulmonary expansion at the time of operation Convalescence was rapid and without incident. Improvement in the functional capacity of the heart was immediately apparent. Ascites did not recur. Injections of mercuzanthin now gave excellent diuresis and were required less frequently. Mobilization was begun within a few days and she was discharged from the hospital after one month. She remained ambulatory and during the next year hospitalization was not required. Auricular fibrillation persisted, for which digitalis was required. She was later trained to give her own subcutaneous injections of thiomerin under her physician's direction. She was able to do her own housework. The ribs did not regenerate. One year after this operation while in apparently good state and in between regular clinic visits she died suddenly. Since auricular fibrillation had been present for many years it was thought that she had died of a massive embolism. The final episode at home was so brief that an accurate account was not secured and an autopsy was not obtained.

It is likely that there are many patients who would be benefited by this operation, but the accounts in the literature of its use are few.

Cardiac Pain in Rheumatic Aortic Stenosis and Aortic Insufficiency

Patients with aortic stenosis and/or aortic insufficiency may have such severe and frequent attacks of angina pectoris that rest and nitroglycerin are ineffective. It may be expedient to resort to the same surgical measures that are employed in the treatment of angina due to coronary artery disease (Chapter 12, p. 292).

Hyperthyroidism

The onset of Graves' disease should be suspected in patients with rheumatic heart disease under the following circumstances: (1) if the heart rate increases after a period of being satisfactorily controlled; (2) if the ventricular rate in the presence of auricular fibrillation increases without apparent explanation, (3) if the ventricular rate in auricular fibrillation can no longer be restored to the optimal level of 70 or 75 per minute by increasing the maintenance dosage of digitalis; (4) if there is unexplained onset of or increase in the degree of failure

The basal metabolic rate should be measured and the blood cholesterol estimated, in order to assay the activity of the thyroid gland It must be kept in mind that the basal metabolic rate may be slightly elevated in patients with congestive heart failure. The measurement of the circulation time may be helpful in these patients. In the presence of congestive heart failure and auricular fibrillation the circulation time is prolonged. A short circulation time or one within the normal range, however, may be evidence that increased thyroid activity is speeding up the circulation It must be kept in mind that activity of rheumatic infection may also cause an increase in the heart rate. The management of hyperthyroidism in patients with rheumatic heart disease and in other cardiac patients is described in Chapter 14

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pressive. The recent application of cortisone and ACTH to the study and treatment of active rheumatic fever opens a dramatic approach which has not been equaled for many years. With the availability of funds for the study of heart disease and interest of competent investigators in rheumatic fever, further study may yield results which will lead to the establishment of the etiology and then the prevention and cure of rheumatic fever.

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CHAPTER 8

Cardiovascular Syphilis

Cardiovascular syphilis usually follows by fifteen or twenty years a primary infection with the disease which has not received prompt and adequate treatment As the highest incidence of primary syphilis is in the early twenties the age group most commonly affected by the cardiovascular form is from thirty-five to fifty.

Aortitis and aneurysmal dilatation of the aorta may occur with or without aortic valvular defect. The aneurysm may be associated with aortic insufficiency and narrowing of the coronary ostia, or these last two may occur alone. The most common cardiovascular lesion is aortic valvular involvement leading to aortic insufficiency. Myocarditis and gumma of the heart are rare.

Approximately one-third of the patients with aortic insufficiency of syphilitic origin have clinical or spinal fluid evidence of neurosyphilis. On the other hand one-fifth of the patients with neurosyphilis have evidence of syphilis of the aorta

If untreated, about 10 per cent of all cases of early syphilis develop cardiovascular syphilis distributed as follows (Webster) about 5 per cent develop uncomplicated aortitis, 2 to 3 per cent develop aortic insufficiency; 1 to 2 per cent develop aneurysm, 0.5 per cent have coronary ostial involvement, 0 2 per cent show syphilitic myocarditis Syphilitic cardiovascular disease occurs more commonly in the Negro than in the white race and more frequently in males than females

DIAGNOSIS

A brief orientation about the diagnosis of cardiovascular syphilis may be in order as a background for treatment

Serologic Diagnosis

Diagnosis may be made easily in most instances when the characteristic lesions have appeared, but it may be difficult in the early cases. The history of the

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but after the onset of symptoms and especially heart failure, the general experience is that the course is more rapidly downhill than in other etiologic types of heart disease.

Aneurysm

An aneurysm arises because of involvement of the medial layer of the artery. The order of frequency of involvement of the portions of the aorta is as follows: ascending aorta, arch, descending aorta in the chest, with the abdominal aorta being the least frequently damaged.

Pain may result because of pressure of the aneurysm on neighboring structures, such as the intercostal nerves. Bone pain may be a consequence of sternal or vertebral erosion Seeping, weeping, or rupture of an aneurysm gives rise to varying signs and symptoms depending on its location and on the structures involved Ruptures into a pulmonary artery and into a bronchus are not uncommon complications. Large aneurysms may be present without causing symptoms but may give appropriate physical signs; other aneurysms cause symptoms, but presenting signs cannot be detected, and in still other instances, neither signs nor symptoms can be elicited

An aneurysm may be present with or without aortic insufficiency. Roentgenograms may reveal its presence but differential diagnosis from other mediastinal shadows is required Angiocardiograms may provide accurate and exact diagnosis. An aneurysm in the absence of aortic insufficiency does not cause cardiac enlargement

Narrowing of the Ostia of the Coronary Arteries

Angina of effort as a manifestation of syphilitic heart disease occurs in aortic insufficiency, but angina may also be due to narrowing of the coronary artery ostia by syphilitic deformity When the deformity has assumed these proportions, however, aortic insufficiency is usually present also Complete occlusion may occur, giving rise to myocardial infarction Electrocardiographic changes may give evidence of restriction of the coronary circulation in addition to those changes associated with the left ventricular hypertrophy of aortic insufficiency Electrocardiograms may show further alterations when myocardial infarction occurs.

Gumma

Gumma of the heart may be suspected when prolongation of the conduction time or symptoms suggestive of complete heart block (Adams-Stokes syndrome) indicate septal involvement

Syphilitic Myocarditis

Syphilitic myocarditis is rare.

TREATMENT

General Discussion

The most important part of the treatment of syphilitic heart disease is its prevention by adequate treatment of early and latent syphilis Treatment which is

syphilitic infection may be of diagnostic value. The serologic test for syphilis is positive in the vast majority of the patients who have never had any specific treatment; it is negative in less than 2 per cent in the general experience The serologic test may be negative even in the presence of cardiovascular syphilis if the patient has had treatment with bismuth, arsenic, or penicillin. In the presence of signs suggesting cardiovascular syphilis, when the serologic test is negative, the detection of other characteristic lesions such as the Argyll-Robertson pupil would be evidence in favor of syphilitic etiology.

Clinical Anatomic Diagnosis

The clinical anatomic lesions of syphilis may be recognized by physical and roentgenographic examination In some instances the electrocardiogram may be used to contribute diagnostic evidence. It may be pointed out that auricular fibrillation is an uncommon complication in cardiovascular syphilis and that subacute bacterial endocarditis is but rarely superimposed upon aortic insufficiency due to syphilis.

Uncomplicated Syphilitic Aortitis

Although some clinicians are of the opinion that this manifestation cannot be detected before aortic insufficiency or aneurysm has developed, most investigators agree that in the absence of hypertension, extensive arteriosclerosis, or rheumatic mitral disease a combination of the following signs and symptoms may be indicative of uncomplicated syphilitic aortitis.

1. *Dilatation of the aorta*, which may be difficult to demonstrate in conventional
size of the
dilatation
ay be the
cause of some dilatation but it rarely reaches the magnitude seen in syphilitic aortitis, and predominates in the descending portion of the aorta. Hypertension gives rise to regular and fusiform dilatation.

2. *Heart failure of the congestive or anginal type, or lowered cardiac reserve* manifested by dyspnea on exertion, in the absence of hypertension or valvular disease.

3. *Localized substernal pain*, dull and aching, not associated with exertion or referred down the arms. It should be differentiated from angina of effort.

4 *Accentuation of the second aortic sound* so that it is tympanitic or bell-like or has a tambour quality.

Syphilitic Aortic Insufficiency

This diagnosis is made when an aortic diastolic murmur is encountered in the absence of rheumatic heart disease. It must be distinguished from calcific aortic stenosis and, less frequently, hypertension with functional aortic insufficiency. Syphilitic aortic insufficiency may be present in a clinically recognizable form for a long time before the appearance of symptoms. The Corrigan pulse, enlargement of the left ventricle, and evidence of left ventricular hypertrophy in the electrocardiogram would appear if the lesion were of adequate proportions. These patients may have angina of effort. Patients with this lesion carry on well for many years

but after the onset of symptoms and especially heart failure, the general experience is that the course is more rapidly downhill than in other etiologic types of heart disease.

Aneurysm

An aneurysm arises because of involvement of the medial layer of the artery. The order of frequency of involvement of the portions of the aorta is as follows. ascending aorta, arch, descending aorta in the chest, with the abdominal aorta being the least frequently damaged.

Pain may result because of pressure of the aneurysm on neighboring structures, such as the intercostal nerves. Bone pain may be a consequence of sternal or vertebral erosion. Seeping, weeping, or rupture of an aneurysm gives rise to varying signs and symptoms depending on its location and on the structures involved Ruptures into a pulmonary artery and into a bronchus are not uncommon complications Large aneurysms may be present without causing symptoms but may give appropriate physical signs, other aneurysms cause symptoms, but presenting signs cannot be detected, and in still other instances, neither signs nor symptoms can be elicited

An aneurysm may be present with or without aortic insufficiency. Roentgenograms may reveal its presence but differential diagnosis from other mediastinal shadows is required Angiocardiograms may provide accurate and exact diagnosis. An aneurysm in the absence of aortic insufficiency does not cause cardiac enlargement

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Gumma of the heart may be suspected when prolongation of the conduction time or symptoms suggestive of complete heart block (Adams-Stokes syndrome) indicate septal involvement.

Syphilitic Myocarditis

Syphilitic myocarditis is rare

TREATMENT

General Discussion

The most important part of the treatment of syphilitic heart disease is its prevention by adequate treatment of early and latent syphilis. Treatment which is

adequate to prevent cardiovascular syphilis in later years may be inadequate to prevent neurosyphilis.

Virulent *Treponema pallidum* organisms have been demonstrated in the aorta in cardiovascular syphilis. Specific therapy directed at the treponemas would be expected then to produce healing of the lesions.

Treatment of cardiovascular syphilis is in a stage of reorientation at the present time owing to the recent application of penicillin to the treatment of syphilis The results from penicillin will have to be as good as or better than from bismuth and arsenicals if its use is finally to be justified. The opinion is general that the use of bismuth and the arsenicals had a beneficial effect.

In a recent study Webster and Reader made a microscopic comparison of the aortas in treated and untreated cases of syphilitic aortitis In all the untreated cases there was evidence of an active syphilitic process, endarteritis, perivascular lymphocytic infiltration, and the presence of plasma cells. Of the adequately treated cases 84 per cent failed to show evidence of activity. The inference is made that adequate treatment with bismuth and the arsenicals brings about arrest of the syphilitic process and consequently relief of symptoms and possibly prolongation of life. Moore is of the opinion that specific therapy prolongs the life of patients suffering from cardiovascular syphilis. He believes that the prognosis in untreated uncomplicated aortitis is good—a matter of many years—but under treatment life is prolonged by 10 to 20 years or better. The duration of life in untreated aortic insufficiency is 2 to 3 years, the average being 30 months, but this is prolonged to 4 to 10 years with treatment. The duration of life in untreated aneurysm ranges from 1 to 3 years, and is on the average 19 months, with adequate treatment life expectancy is stretched to 5 to 10 years. Statistics relating to coronary ostial involvement are not available. The recent analysis of the New York Hospital statistics by Webster and Reader also indicates the beneficial effect of adequate treatment on cardiovascular syphilis.

The treatment of cardiovascular syphilis today is by the use of penicillin. In addition reliance is now placed upon the curative properties of penicillin in the primary and latent forms of the disease to prevent the later development of cardiovascular disease. It must be kept in mind, however, that it will be twenty years or so before the effect of penicillin on the prevention of cardiovascular syphilis can be ascertained. The pooled experience of large clinics is being utilized to provide adequate case loads upon which a satisfactory evaluation of therapy can be based.

The *objectives of treatment* in cardiovascular syphilis are: to arrest the progress of the disease, to relieve the patient's symptoms, and to prolong life. Restoration of cardiac pathology to a normal status is not possible. Careful neurologic examination of the patient as well as tests of the spinal fluid should be made to detect the presence of neurosyphilis before beginning specific treatment.

Specific Measures

Since the penicillin therapy of cardiovascular syphilis has for the most part replaced the use of bismuth and arsenicals, regimens relating to the latter will not be given They are amply recorded in many textbooks for historical and reference purposes.

Penicillin

In the application of penicillin to cardiovascular syphilis, investigators have reasoned by analogy from the effects of the drug in other situations, since it is effective in the healing of other early and late lesions of syphilis. They are of the opinion that the drug should be effective, but are aware of the fact that it will require many years to collect adequate evidence that this is the case.

The expense to the patient of a course of penicillin therapy may appear greater [illegible]

REGIMEN. The following regimen is now in use at the New York Hospital for the treatment of cardiovascular syphilis in the clinics (Table VI):

Table VI. Treatment of All Forms of Cardiovascular Syphilis
(Aortitis, Aneurysm, Aortic Involvement, Coronary Ostial Involvement, and their Combinations)

Weeks	*Penicillin Schedule*	*General*
1st to 2nd incl	Procaine penicillin G, 300,000 units intramuscularly daily	Hospitalized, but limited activity*
3rd to 12th incl	Procaine penicillin G, 300,000 units intramuscularly twice a week	Ambulatory

* Hospitalization may not be necessary for all patients, some may remain ambulatory

1 The patient is hospitalized for the first two weeks of therapy During this time activity is limited but he is allowed to be up around the pavilion. Recent experience has indicated that hospitalization may not be necessary for all patients, or for the full period if the earlier part of the treatment was without incident.

2 Procaine penicillin G, 300,000 units, is given intramuscularly daily for two weeks The slow absorption of the procaine derivative provides an adequate blood level of penicillin for 24 hours

3 For the next ten weeks 300,000 units of procaine penicillin G are given intramuscularly twice a week, the patient being ambulatory.

All forms of cardiovascular syphilis, namely aortitis, aneurysm, aortic insufficiency, coronary artery involvement, and combinations of these are treated according to this penicillin regimen.

The amount of penicillin which is used for cardiovascular syphilis is ample also for the treatment of central nervous system syphilis, should this complication be present, since it is given in larger amounts and over a longer period of time than the treatment of central nervous system syphilis requires.

During treatment careful observation detects changing physical signs which might indicate the development of aortic insufficiency or progression of the

disease. Occasional electrocardiograms and two-meter roentgenograms are useful in detecting myocardial alterations and changes in the size and shape of the heart and aorta.

Patients are followed at frequent intervals after completing the course of penicillin It is not known at this stage of follow-up whether a second course of the antibiotic may on occasion be necessary.

REACTIONS. It has been indicated that penicillin has replaced bismuth and the arsenicals in the treatment of cardiovascular syphilis. A few clinics, however, recommend a preliminary course of bismuth and iodide before the use of penicillin.

Reactions are encountered infrequently with the use of penicillin as contrasted with bismuth and arsenicals.

Sudden death occurred occasionally during the intravenous injection of old arsphenamine; a toxic effect on the myocardium probably induced ventricular fibrillation. This reaction is not expected with penicillin.

Occasionally in the use of the bismuth-arsenical regimen, the so-called *Jarisch-Herxheimer* reaction occurs. This is an exacerbation of the syphilitic lesion a few hours after the intravenous injection of the arsenical. It is also called "therapeutic shock" It is to prevent this reaction that a course of bismuth was given before the addition of the arsenical; this provides for a slow healing in the early stages of treatment instead of the rapid alterations which may occur after arsenic. Apparently there have been no clear-cut instances of the Jarisch-Herxheimer reaction following the use of penicillin, although a few moderate febrile reactions have been reported. When penicillin was first used in the treatment of cardiovascular syphilis, small amounts, namely 1000 units every three hours for two to three days, were given as preparatory treatment before the institution of larger doses In other instances several weeks (four at a minimum) of bismuth therapy preceded the use of penicillin. The regimens now in use provide for full doses at the beginning of therapy.

Although a great deal has been written about the so-called *therapeutic paradox* many of the physicians who have had a large experience in the treatment of cardiovascular syphilis doubt that the phenomenon actually occurs. It is unlikely that too rapid healing causes incapacitating scar formation, the rapid appearance of aortic insufficiency, or serious impairment of the coronary circulation by deformity of the openings of the coronary arteries.

Iodides

There appears to be no good reason for using iodides in the treatment of cardiovascular syphilis It is difficult to find adequate supportive evidence, except the historical background, that they have any beneficial effect.

Treatment of Associated Conditions

Congestive Heart Failure

It was formerly thought that specific antisyphilitic therapy should be instituted only if there were no evidences of cardiac decompensation. Recent observations made by Stokes indicate that this precaution is not necessary. Treatment with penicillin is started at the same time that measures are directed at the restoration

and maintenance of compensation. The same measures are used in the treatment of heart failure caused by syphilitic heart disease as are used in other types of heart disease.

The onset of heart failure during antisyphilitic treatment would, however, be an indication for the temporary discontinuance of the specific therapy.

Angina Pectoris

Angina due to syphilitic heart disease is treated like any other type of angina pectoris, by the use of vasodilators and management of the patient's physical and mental activities (Chapter 12). The presence of angina offers no contraindication to the institution or maintenance of specific therapy with penicillin.

Myocardial Infarction

The onset of cardic *pain* during specific antisyphilitic therapy should warn the physician to be on guard for the possibility of myocardial infarction which may have resulted from narrowing, deformity, or closure of the coronary ostia When this complication occurs specific therapy is discontinued and the regimen used in the treatment of myocardial infarction is promptly instituted (Chapter 13).

Rupture of Aortic Aneurysm

The physician is indeed helpless to provide any permanent relief when this complication occurs The weeping of blood into a bronchus or the esophagus indicates that erosion of a larger vessel in these areas may occur at any time The aneurysm may rupture into the mediastinum or into a pulmonary artery with consequent pain, shock, and perhaps sudden death. Emergency measures are applied as the situation dictates When there is moderate weeping the patient should be kept quiet, morphine should be given liberally to insure rest and to allay apprehension With moderate fall in blood pressure a clot may form over the eroded area and the slow loss of blood may cease. This may be only temporary, however, since

Follow up Care

Close continued observation of patients with syphilitic cardiovascular disease after completion of specific therapy serves not only to detect untoward signs and symptoms and the appearance of other syphilitic manifestations, but also to deter the patient from prolonged physical activities which might be harmful. If the disease has not progressed to the point where gainful work is contraindicated, the patient should be advised about work which is suitable and within the functional capacity of his heart Attempts should be made to relocate the patient in such activities.

Surgical Treatment of Aneurysms of the Aorta

When aneurysm of the aorta is first detected it may have progressed to a stage in which the dilatation is so marked and the wall so thin that the integrity of the

vessel is compromised and danger of rupture or dissection is always present. Therapy may result in disappearance of the signs of activity—according to evidence gained from postmortem microscopic examination of the aorta—but restoration of continuity of the layers of the vessel is not to be expected.

Blakemore has reported on the surgical treatment of saccular aneurysms. He has accepted the premise that a blood clot in the aneurysm with its subsequent replacement with scar tissue strengthens the wall and may prevent its rupture. He has induced clotting of blood in the following way: Small gauge silver wire is threaded through a needle and pushed on into the aneurysm. The wire coils up in the sac and forms a mesh. When an appropriate length has been placed in the sac an electric current is passed through the wire. This induces clotting of the blood in the sac. He has reported a certain degree of success with this method of treatment but I am not aware that it has been used extensively by other surgeons.

Recently Poppe has reported the *cellophane treatment* in 6 patients with syphilitic aneurysms. Wrapping the aortic aneurysms with polythene cellophane produced a dense fibrous tissue reaction which reduced the pulsation, expansion, and tendency to rupture. He reported that pain was also relieved.

In certain circumstances it may be possible in the future to resect the aneurysm and replace it with a segment of normal vessel from a blood vessel bank. This has been accomplished in the treatment of coarctation of the aorta. However, in the reported series blood was already by-passing the obstruction so that interruption of blood supply was not required. Moreover vessel repair in the older age group in which aneurysms due to syphilis occur is more difficult due to arteriosclerotic changes

SUMMARY

Syphilitic cardiovascular disease is preventable by the adequate treatment of primary and latent syphilis by bismuth and arsenic We shall not know for two decades or so whether penicillin will have also prevented the late occurrence of cardiovascular syphilis, since these complications arise ten to twenty years after the initial infection in untreated or inadequately treated patients The cardiac manifestations of syphilis relate for the most part to the aorta and the aortic valves. Adequate treatment of cardiovascular syphilis with bismuth and arsenicals according to most observers has increased the life span of patients in all categories: aortitis, aneurysms, and aortic insufficiency. Treatment destroys the organism and results in healing with scar formation, so that the progress of the disease is arrested. Treatment cannot, however, restore the continuity of the vessel layers nor restore function to incompetent valves. Careful supervision of the patient with appropriate therapy minimizes and may prevent or delay the onset of heart failure and other manifestations resulting from anatomic deformity

It may not be necessary to delay specific therapy if heart failure is present. Angina pectoris is not a contraindication to the use of penicillin. Untoward reactions from the use of penicillin are apparently rare so that full doses may be given at the beginning of treatment.

With the healing of the syphilitic lesions the scarring and original defect remain

and will require continued efforts at alleviation or repair: aneurysm, aortic insufficiency, coronary ostial narrowing Surgeons have become interested in these manifestations. Clotting has been promoted in saccular aneurysms so that scar tissue can strengthen the thinning wall. Encirclement of the saccular aneurysm with cellophane has been used to induce the formation of scar tissue with the attainment of similar ends.

The extensive interest in the eradication of venereal disease by federal and municipal agencies and the general population, together with the wide availability

It will be a major therapeutic triumph if the syphilitic lesions in cardiovascular syphilis can be so quickly and so easily arrested, but it will remain for other approaches to cope with the anatomic defects which remain.

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[illegible] REYNOLDS, F. W.

for life insurance

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vessel is compromised and danger of rupture or dissection is always present. Therapy may result in disappearance of the signs of activity—according to evidence gained from postmortem microscopic examination of the aorta—but restoration of continuity of the layers of the vessel is not to be expected.

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SUMMARY

Syphilitic cardiovascular disease is preventable by the adequate treatment of primary and latent syphilis by bismuth and arsenic. We shall not know for two decades or so whether penicillin will have also prevented the late occurrence of cardiovascular syphilis, since these complications arise ten to twenty years after the initial infection in untreated or inadequately treated patients. The cardiac manifestations of syphilis relate for the most part to the aorta and the aortic valves. Adequate treatment of cardiovascular syphilis with bismuth and arsenicals according to most observers has increased the life span of patients in all categories: aortitis, aneurysms, and aortic insufficiency Treatment destroys the organism and results in healing with scar formation, so that the progress of the disease is arrested Treatment cannot, however, restore the continuity of the vessel layers nor restore function to incompetent valves Careful supervision of the patient with appropriate therapy minimizes and may prevent or delay the onset of heart failure and other manifestations resulting from anatomic deformity.

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With the healing of the syphilitic lesions the scarring and original defect remain

CHAPTER 9

Hypertension and Heart Disease Due to Hypertension

Hypertension is said to be present when the resting systolic level is over 140 mm Hg and the diastolic more than 90 mm It is classified as *essential hypertension* when unassociated with any demonstrable disease, when a definite cause cannot be determined, and when there is no history of preceding renal damage in a patient in the early decades.

CLINICAL COURSE

The courses which may be followed in patients with hypertension are shown in the diagram in Figure 37 At the onset the renal function is normal, the heart size is not large, and evidences of vascular damage cannot be detected either in the peripheral vessels or in the eyegrounds. Hypertension is one of the common causes of heart disease, although the cardiac manifestations do not usually appear for several years In these cases the heart has generally developed left ventricular hypertrophy to compensate for the additional work created by the high diastolic pressure Loss of compensation may be manifested in several ways. the heart may not be able to sustain sudden prolonged rises in blood pressure and develop acute heart failure This may progress to recurring incidents of acute cardiac failure with rapid restoration of compensation or the chronic form of congestive heart failure Usually decompensation occurs not only as a result of the burden of the hypertension per se but also because, by this time, arteriosclerotic changes have impaired the coronary circulation and perhaps caused angina and myocardial infarction

In x-ray photographs of the chest the heart takes on the typical boot shape with a possible widening of the aorta. The electrocardiogram eventually demonstrates

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in those dogs with chronic hypertension and renal damage, removal of the affected kidney—resulted in fall in blood pressure. This technic induced morphologic changes similar to those in essential hypertension of long standing in man. The relationship between the Goldblatt phenomenon and essential hypertension as it is seen clinically in man is, however, still not clearly defined. The finding of vasoexcitor material by Shorr and his associates in the blood of patients with hypertension as well as in Goldblatt animals provides a link which may be strengthened by further evidence. Castleman and Smithwick have shown that in early essential hypertension the anatomic and microscopic structure of the kidneys does not differ from that seen in normal individuals It may be, however, that physiologic changes precede morphologic abnormalities, or that the present microscopic technics do not detect early but nevertheless significant changes. The second possibility has been strengthened by the recent observation by Shorr and his associates of differences between the normal kidney and the Goldblatt kidney using microhistochemical technics.

Selye's suggestion that hypertension may arise as an adaptation phenomenon is of interest but has no practical application with respect to etiology The attempts to relate the adrenal cortex to hypertension have not been convincing

The fall in blood pressure in patients with hypertension after anterior root section and lumbodorsal sympathectomy does not throw any light on the mechanism of essential hypertension and does not argue for a neurogenic mechanism

The hypothesis of psychiatrists and those interested in psychosomatic medicine that essential hypertension results from conflicts and tension states remains unproven

The etiology of hypertension being unknown, the treatment is empirical Since the characteristic by which hypertension is recognized is the elevation of systolic and of diastolic pressures, it is natural that treatment should be directed at the correction of this defect

CAUSES OF HYPERTENSION OTHER THAN THE ESSENTIAL TYPE

The most common variety of hypertension is that known as "essential hypertension" However, if rise in blood pressure from any cause is maintained over a long enough time all of the cardiac consequences may be sustained which have been mentioned as following the essential variety.

When persistent hypertension is found, the cause must be discovered before specific therapy is undertaken Causes of hypertension other than the essential type are as follows (1) glomerulonephritis, (2) pyelonephritis; (3) polycystic kidney disease, (4) coarctation of the aorta (Chapter 6), (5) pheochromocytoma; (6) Cushing's disease, (7) compensatory rise in blood pressure in aortic insufficiency; (8) hyperthyroidism, (9) periarteritis nodosa (Chapter 18), (10) localized narrowing of a renal artery by localized arteriosclerosis or by external compression; (11) aneurysm of a renal artery, (12) urinary obstruction caused by renal calculi or pressure on a ureter giving rise to hydronephrosis, (13) prostatic enlargement; (14) increase in intracranial pressure; and (15) blast hypertension

left axis deviation, and the unipolar limb leads and chest leads may show evidence of the left ventricular hypertrophy. Later, intraventricular conduction defect may appear. *Auricular fibrillation is relatively uncommon.*

In other patients hypertension may cause the most profound changes in the

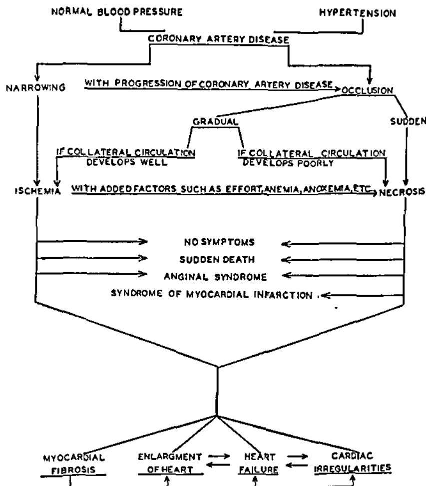


FIG 37

The Natural History of Coronary Artery Disease

brain or the kidneys and in other patients still all of these systems may be involved. The complication of dissecting aneurysm of the aorta is discussed on page 363

ETIOLOGY

It has long been thought that the kidneys were linked in some way with the production and maintenance of hypertension This view was strengthened by the observations of Goldblatt and his associates, who induced sustained hypertension by partial constriction of a renal artery in dogs. Release of the constriction—or,

This drug should be used only on patients with good renal function. If it is used the blood level should be estimated every week and the dosage adjusted so that it does not rise above 10 mg. per 100 cc; it should be kept in the range of 5 to 8 mg. Some such dosage as follows has been recommended 0.1 Gm. three times a day after meals for one week, then twice a day for one week, then once a day for one week, and from there on a schedule of once a day or every other day. As has been indicated, in a certain number of patients a fall in blood pressure and moderation of symptoms ensue. The course of the disease is unchanged, however, by the drug.

Bismuth subnitrate 0.6 Gm three times a day has been used This drug may result in toxic symptoms and cerebral accidents have followed its use. Its use is therefore not recommended.

Erythrol tetranitrate in 0.03-Gm. doses has been used but is not recommended.

Tetraethylammonium chloride (Etamon) has no place in the daily management of hypertension

Penta- and hexamethonium salts Methonium compounds, like tetraethylammonium, act by blocking nervous impulses at the autonomic ganglia A few reports have been made of their use in the medical treatment of hypertension (Page, Smirk, Campbell and Robertson) They lower blood pressure but they have undesirable side effects. Page states that the minimal dose of pentamethonium to produce a fall of 40 to 50 mm. Hg systolic pressure varies from 5 to 150 mg subcutaneously, hexamethonium may be given by mouth in small doses increased progressively up to as much as 500 mg. four to six times a day. Freis *et al.* found that the most effective and best tolerated schedule was the subcutaneous injection of hexamethonium at intervals of 12 hours in doses of 10 to 75 mg. of the ion, depending on the response, with the oral administration of 50 to 150 mg. of 1-hydrazinophthalazine midway between the doses of hexamethonium, together with a 200- to 500-mg sodium diet per day Undesirable reactions were: occasional severe reduction of blood pressure after the initial injection, postural hypotension, gastrointestinal atony and difficulty in urination. The sensitivity of the blood pressure to these drugs is said to be increased by the use of a low sodium diet The place of these drugs in the management of patients with hypertension has not been established

1-Hydrazinophthalazine. Schroeder has found that the administration of 1-hydrazinophthalazine gave significant lowering of the blood pressure, but rarely to normotensive levels, without deleterious effects on the heart and kidneys. He gave 50 to 150 mg every four to six hours to hospitalized patients and three to five times a day to ambulatory patients Use of this drug may be combined with hexamethonium and a low sodium diet

Veratrum viride. Recent studies have been made of the use of veratrum viride and purified extracts of this substance. This is at present in the experimental stage. The blood pressure is lowered transiently. Whether the hypotensive effects are sufficiently predictable for ration doses to be used as a safe form of therapy is not yet certain. Alkaloids have been prepared under the names of Veratrone and Veriloid. It is recalled that veratrum viride also induces bradycardia

The use of *pyrogens* in lowering the blood pressure in hypertensive subjects is of interest but has no wide field of application in the treatment of these patients

TREATMENT OF ESSENTIAL HYPERTENSION

Estimate should be made of. (1) the state of the kidneys by tests of renal function, (2) the state of the heart. An electrocardiogram may give evidence of myocardial damage and allow inferences to be made about the coronary arteries Two-meter x-ray photographs of the heart reveal the degree of cardiac enlargement. An estimate of the functional capacity of the heart can be made from an analysis of how much the patient is able to do; (3) the state of the eyegrounds; (4) the state of the peripheral vessels; (5) the emotional health of the subject, the family and home life, the work-a-day life, recreations, and interests; (6) the familial incidence of hypertension (hypertension may be a hereditary disease conveyed as a mendelian dominant); (7) the duration of hypertension, and (8) the blood pressure levels and their fluctuations.

A sufficient number of blood pressure readings should be taken over a long enough period to be certain that the patient has hypertension and to eliminate the possibility of transient rises in the earlier recordings, although there are circumstances in which importance is to be attached to these transient rises Levy, in a cooperative study, has shown that (1) the frequency of transient hypertension increases with age, (2) *sustained hypertension occurs more frequently* in patients with a history of previous transient hypertension, (3) the death rate from cardiovascular disease is higher in patients with a history of transient hypertension; (4) slight degrees of elevation are important even when the systolic level alone is implicated; (5) a transient rise in diastolic pressure above 100 mm. is of greatest significance; (6) but the height of temporary rises is of no prognostic significance. (7) patients with transient rises show higher rates for later sustained hypertension, (8) when both transient tachycardia and transient hypertension are present, the incidence of later sustained hypertension is twice as great as when either is present alone, (9) transient tachycardia due to emotional disturbance or some other cause not discernible, like transient hypertension of similar origin, is often the precursor of hypertensive vascular disease.

Treatment by Drugs

Potassium thiocyanate or *potassium sulfocyanate* has had a certain vogue. Approximately 30 to 50 per cent of patients experience fall in blood pressure from its use. I have not been convinced from my own limited experience with the drug or by the published reports that it is sufficiently effective to warrant the risks associated with its use. The *following toxic effects have been observed: pain in the jaws,* sensitivity of the teeth, ulnar palsy (all attributed to peripheral neuritis), psychoses and mental confusion, thrombophlebitis, angina pectoris and coronary thrombosis,

strongest advocates of this drug, pointed out that thiocyanate causes satisfactory reduction of blood pressure in more than one-third of the patients but that the drug *is dangerous* and that not even the precaution of obtaining frequent blood levels will prevent occasional fatal intoxication

centration of the plasma rose, while the sodium did not change significantly; the heart became smaller, the electrocardiogram may show regression in the degree of left axis deviation and disappearance of negativity of $T_{1,2}$ and T_4; bundle branch block may disappear, vascular retinopathy with papilledema, hemorrhages, and exudates may disappear. There was an average weight loss of around ten pounds.

In many cases who respond favorably, additions to the diet such as small amounts of nonleguminous vegetables, potato, lean meat, chicken, or fish are permitted after two to five months. These additions reduce the effectiveness of the regimen, and if the improvement which has been secured on the full rice diet is not maintained, the strict regimen is again instituted

Patients who are given the rice diet should be kept under close supervision to detect any untoward effects. Symptoms of salt depletion should be looked for.

Contraindications to the use of the rice diet are: increase in nonprotein nitrogen, heart failure, serious vascular disease, and uremia.

CRITIQUE. In a limited experience, I have not seen enough benefit to warrant the general use of this diet in the treatment of hypertension. It is a relatively easy way to provide a salt-poor diet but it should not be continued for too long. When the rice diet regimen is being carried out extensively in a community, part of the benefit may result from mass psychology, from the faith which may have been engendered by reports of friends and by publicity, and from a regimen which takes patients away from their usual business, from their family, and from sources of annoyance in their daily lives

There have been varying opinions expressed by those with experience in the use of the rice diet Contratto and Rogers think that the diet offers the greatest hope for the medical treatment of hypertension They do not contend that the benefits result from weight loss but think that the low sodium content of the diet plays a role

A recent report of Williamson points up the difficulties in evaluating this regimen fall in blood pressure during adequate control periods, which would have been counted as successes for the diet if it had been inaugurated without the control period, refusal of patients to follow the diet, untoward effects of the diet requiring it to be discontinued, and its unsuitability for many ill patients Only 11 of 20 patients finally admitted to the study followed the regimen for six weeks or more Only 4 of these demonstrated a significant decrease in diastolic blood pressure The addition of salt-free protein and fat to the diets of 3 of these 4 patients did not result in any change in blood pressure or symptomatology The administration of sodium chloride was followed by a rise in systolic blood pressure of 20 mm in 1 of the 4 patients and equivocal rises in 2 others. These latter observations indicate that sodium chloride restriction may play a significant role in lowering of blood pressure by the rice diet

In reports which have appeared from other clinics, no striking declines in blood pressure have been noted In any attempt to duplicate Kempner's results the regimen should be carried out precisely according to his regimen, so that the comparison can be made exactly It may be that the benefit to be expected in its routine use lies somewhere between Kempner's enthusiastic reports and the much less successful results of other investigators. Certainly it is not the answer to the

Diets

Low Salt Diet

For many years clinicians have used a low salt diet in the regimen of patients with hypertension. Recently interest and enthusiasm for the low salt diet in this connection have been renewed. Certain patients subjected to such a regimen experience some fall in blood pressure, but it rarely assumes normal levels. There may be relief of symptoms, but for most patients the benefits are meager and disappointing.

A diet containing only 200 mg. of sodium daily may be necessary to achieve significant lowering of blood pressure. While the sodium ion may be in some way related to the mechanism of hypertension rigid restriction of the sodium chloride intake is justified only in rare instances. The harm of rigid deprivation may outweigh the benefit.

Usually I have advised patients to take a diet containing approximately 2.0 Gm. of sodium chloride daily For other patients I may restrict salt only to the amount used in cooking, no extra salt being added to the food at the table Salt restriction can be achieved by using regular food prepared without salt. Highly salted foods such as fish are not allowed The diet should contain meat and eggs daily. Because of the sodium chloride in meat it may be necessary to use Lonalac as a protein substitute in place of part of the meat. Vegetables are cooked without salt, and those having a high salt content are boiled several times before being served. Salt-free bread and butter can be obtained easily. Owing to their salt content milk and cream can be used in only small amounts. Seasonings which are nonsalty may make the food more palatable, but salt substitutes containing potassium and lithium should be avoided Cationic exchange resins may be used occasionally as adjuvants to sodium-poor diets (see p 17) and to thoracolumbar sympathectomy.

The organization of salt-poor diets is discussed in Chapter 34.

On such regimens the blood pressure sometimes falls It might be that the combination of low salt diet, for what benefit it may give, and other measures which are advocated, would result in enough lowering of blood pressure and alleviation of symptoms to make the effort worth while. Declines in blood pressure can be recorded with each period of restriction of the salt intake in certain patients, with rises in blood pressure when salt is added

Rice Diet

Recently the so-called rice diet has had a wide vogue. This diet consists of boiled rice, fruit juices, and supplemental vitamins The rice diet advocated by Kempner contains 2000 calories, not more than 5.0 Gm of fat, approximately 20.0 Gm of protein, not more than 200 mg. of chloride, and 150 mg. of sodium. The fluid intake is restricted to around one liter per day. Although the diet is deficient in protein and electrolytes patients apparently remain in nitrogen balance. Whatever benefits might accrue from its use are probably to be attributed to its low sodium content but may be due in part to its low nitrogen and low caloric values. Kempner has reported fall in systolic and diastolic blood pressures, the blood urea nitrogen fell, the blood cholesterol declined, the plasma chlorides fell, the potassium con-

in treatment might well be to lower it or to restore it to normal levels. Nevertheless, in testing any drug or procedure it must be kept in mind that the effects are difficult to evaluate because of fluctuations in blood pressure without medication and because of the relief patients experience when they are given any kind of medication, care, and attention.

The place of salt-poor and rice diets has already been discussed on p. 254

If the patient is overweight the caloric intake should be reduced and a program directed at a gradual loss of weight. This can be conducted without the omission of any of the essential factors in the diet. Hypertension in the obese person is caused by the same factors as in the nonobese. Obesity is only an aggravating factor, which should be minimized by judicious reduction in weight.

Regular *bowel habits* should be encouraged

The moderate use of *alcohol* promotes vasodilatation and relaxation and should be encouraged It is contraindicated if it produces side-effects such as pounding of the heart For most persons who are gainfully employed its use has to be limited to after-work hours, before dinner and perhaps later in the evening. If the patient is obese, its effect on increasing appetite must be considered

I usually advise against the use of *tobacco* It may induce effects which it would be best to avoid increase in heart rate, increase in blood pressure, decrease in peripheral blood flow due to vasoconstriction. In certain susceptible individuals smoking may be correlated with alterations in T waves similar to those seen in anoxemia

Phenobarbital may be used to give relief from headaches due to hypertension To certain patients 0 16 to 0 32 Gm may be given three to four times a day to lower the hyperactivity of the patient and ease tensions Moderate fall in blood pressure may result It is one of the most useful drugs available for the care of hypertensive patients

Elimination of *overwork and overdrive*, overeating, overdrinking, and of too little sleep is beneficial.

The patient's work should be discussed with him and a more suitable job advised if necessary

Strenuous exercise and sports are discouraged, but the less active recreations may be permitted depending on the level and duration of the hypertension, the age of the patient, and his functional capacity The recommendations in each patient must be individualized

Measures are directed toward *relaxation* Part of this may be secured by psychotherapy and part by re-education of the patient through his own efforts. He should learn to lower the pace at which he lives and level off the peaks of his reactions to his environment The patient should be encouraged to see the wisdom of a longer life and of postponement of invalidism which would result from a slight restriction of activity There is no occasion for bed rest for patients with hypertension without complications, unless the blood pressure is at dangerously high levels, or a regimen is being evaluated in which activity might hinder objective estimations. Patients with uremia should be kept mobilized within the limits of their capacity

Warm baths at night may be relaxing. I have had no controlled experience with

medical treatment of hypertension. The diet may be given a trial when other forms of treatment have not been beneficial and when the patient is not suitable for sympathectomy.

Dehydration

There has been some discussion of dehydration as a treatment for hypertension. Dehydration is a deleterious state for the body and is looked upon by clinicians as a state to be corrected by restoration of fluid balance. Patients should not be dehydrated Instances in which fall in blood pressure has resulted from dehydration by the use of mercurial diuretics are probably examples of patients suffering from concurrent heart failure; the blood pressure fell with restoration of compensation even though excretion of fluid proceeded to the deleterious side, namely dehydration. It has long been known that heart failure may cause either a fall or a rise in blood pressure, recovery of compensation is followed by restoration of the blood pressure to its usual levels. Moreover, in those patients with whom a dehydration regimen was used there may have been other factors prevailing in the treatment which influenced the fall in blood pressure. The mercurial diuretics have been used to accelerate the excretion of sodium—a practice in the treatment of hypertension to which I do not subscribe.

MANAGEMENT OF PATIENTS

What to Tell the Patient

Very early in the management of the patient an assessment of the patient's relation to his family and his work should be made Frank discussion on the part of the patient should be encouraged so that the part which tension states and conflicts play in the elevation of the blood pressure may be ascertained and evaluated.

First, *should the patient be told that his blood pressure is elevated?* It may be best not to tell patients about moderate elevations if they are to remain under supervision and return at intervals for follow-up. If there is the chance that the patient may go to another physician who may disclose the moderate elevation of blood pressure, it may be best that the patient be apprised of it at this time. When the patient is not told about the elevation of blood pressure, it should be discussed with a member of the family When the patient is told about the hypertension, it should be discussed in terms which are not alarming, and with immediate reassurance. It is a common experience to see a patient without symptoms until he is told he has high blood pressure. I usually do not report the levels of blood pressure to the patient; I tell him at the start that it is not my custom to do this The patient may be reassured at each visit without placing emphasis on the level of blood pressure One often finds that the symptoms are not related to the level of blood pressure, for instance, headache may occur at higher or lower levels of blood pressure at different times. It is not uncommon to have a patient state "I know you will find my blood pressure down this morning, I feel so well" only to find that the blood pressure is higher than on the previous visit.

Since elevation of blood pressure is the signpost of the disease, the chief objective

of a patient with hypertension requires time of the physician but the responsibility is clear.

Jacobson's book, *You Must Relax*, written for the laity, may be of some help to patients in training them to relax and to eliminate tensions. Mass psychotherapy attempted in classes planned for hypertensives has met with moderate success in

[illegible] ably the [illegible] e of the hypertensive predisposition is as strong as some investigators indicate, it is hard to see how these nonspecific measures could reverse this tide. On the other hand if we make the subjects more comfortable and happier individuals, if they can avoid some of the mental and physical stresses which precipitate complications, and if we have taught patients to live with their hypertension, it will have been worth while.

TREATMENT OF CARDIAC COMPLICATIONS OF HYPERTENSION

Acute Heart Failure with Pulmonary Edema

Patients with hypertension are subject to acute heart failure with pulmonary edema This may be brought about by sudden or prolonged exertion such as walking upstairs, lifting heavy objects, running, and childbirth or by any sudden rise in blood pressure—so-called hypertensive crisis The treatment of this complication is described in Chapter 1 Hypertensive patients should be warned against events which precipitate failure They are prone to have attacks of nocturnal dyspnea or pulmonary edema and may require regular injections of a mercurial diuretic to prevent these symptoms.

It should be remembered that patients with pheochromocytoma also exhibit paroxysmal rises in blood pressure leading to acute pulmonary edema.

Chronic Congestive Heart Failure

With some patients the development of dyspnea on effort will lead to gradual or rapid increase of chronic congestive heart failure. After restoration of compensation by the methods outlined in Chapter 1 patients may return to high levels of activity if their regimens are closely supervised With heart failure the blood pressure may rise or fall, it is restored to its usual hypertensive levels when compensation returns. During heart failure the basal metabolic rate may be elevated, then fall with restoration of compensation.

SURGICAL TREATMENT OF HYPERTENSION

The surgical treatment of hypertension has been employed increasingly in the last few years The principle of all these operations is the section of the vasoconstrictor nerves supplying the large splanchnic area and the lower extremities Since they are employed in patients usually considered as having a medical disease and are frequently undertaken at the request of the physician, it is well for the internist

spa therapy. Patients who "take the cure" may feel better because of the routine, the new atmosphere, the holiday or vacation attitude, and the provision for adequate sleep at night. These objectives might be difficult to obtain with the patient in a hospital or his home.

Busy executives may find it possible to lie down in their offices after lunch Business should not be planned for the lunch period.

Adequate sleep. Inability to sleep may be a pronounced symptom of the tension in these subjects, as a regimen is effected there may be improvement. When quick-acting drugs—pentobarbital 0.1 Gm. or the longer acting phenobarbital 0.32 Gm —are used to aid sleep, the *patient should not be allowed to become anxious* about their use. It may be more expedient to take the medication and have a restful night, than to lie awake with the anxiety about the approaching day's work without adequate sleep. Inability to sleep may be a symptom of anxiety which may be eliminated as the patient gains some insight.

The home life should be given attention. its organization, the patient's role in it, and its effects on him. With a little thought changes may be instituted which may be beneficial. Frequent short vacations may be helpful when they can be arranged. Exposure to hot sun should be avoided Bathing in moderately warm water may be relaxing, but cold water and cold showers should be avoided, even when the patient thinks he "reacts" favorably to them. Patients who have acquired distorted ideas about the dangers of hypertension should be reassured regarding the prognosis and the rationale of the regimen which is being set up A hobby may be used to encourage relaxation and to provide a contrast to the daily work.

Psychotherapy

Every successful physician treats the "whole patient" whether or not he calls this psychotherapy In certain instances the skill and technics of a trained psychiatrist are required, in most, the sympathetic and alert physician can achieve the same benefits if he will devote the necessary time to it, without the disadvantage of losing the benefits of the original doctor-patient relationship. Patients may feel better by having the psychosomatic aspects of the disease discussed with them and may gain an insight into their problems, but the blood pressure may remain unchanged.

The best results are obtained by listening to the patients' troubles, guiding them in rearrangement of activities and life as needed, and trying to let the patients arrive at the decisions themselves. They should be made to feel that no problem is too trivial to ask for the physician's help, as it is often the small ones that are magnified and assume large proportions so that they get out of focus in the patient's vision.

These patients are susceptible to encouragement. They should not have the notion that nothing can be done for them and that the physician is not interested. If this is allowed to come about they begin the rounds from one physician to another, being given attention at first as a "new case," followed later by the physician's waning interest. It is partly the physician's fault that these patients finally take up with fads and with each newly publicized "cure." The management

More recently *complete bilateral sympathectomy* has been done in certain patients with hypertension, especially those with angina. Poppen's technic allows of an exposure for the removal of the sympathetic system from the fourth thoracic to the third lumbar ganglion inclusive

Ray has 29 cases in which total bilateral sympathectomy from the stellate ganglion to L_3 has been performed This operation appeared appropriate for the following types of patients:

1. *Patients with high blood pressure who suffered also from angina* The lumbodorsal sympathectomy provided for lowering of blood pressure and the stellate cervical sympathectomy provided for the relief from angina (Chapter 12). Ray has extended this procedure to 20 patients.

2 *Patients who exhibited persistent tachycardia and palpitation* after the Smithwick operation.

3. *Patients who developed persistent, disagreeable Raynaud's disease* of the upper extremities after the Smithwick operation

4 A few patients in the *malignant* phase of hypertension *without cardiac symptoms.*

Completely sympathectomized patients manage very well The heart rate falls to around 50 to 60 per minute at rest, at exercise it rises perhaps to 70 per minute, with a maximum of 80 per minute These patients are unable to cope with extremes of heat or cold as well as are normal subjects.

The results from the pooled experiences with sympathectomy are difficult to classify owing to different types of operation, to different classifications of cases operated, and to different criteria and different procedures in the analysis of the data But roughly something like the following results may be expected·

The blood pressure is lowered to normal limits in a number of patients—approximately one quarter—after operation and is maintained for varying lengths of time The lowering may be very marked but not quite to normal in about one quarter of the patients and moderate in the third quarter. The last quarter may exhibit no essential change In some patients the fall in blood pressure after operation will be satisfactory but after six months to one year or longer there is a progressive slow rise

The operative *mortality* in experienced hands and with carefully selected cases should not be more than 2 per cent In patients with marked to moderate fall in blood pressure all or most of the symptoms and signs related to the hypertension may disappear Headaches vanish, retinal hemorrhage and papilledema regress and [illegible] regardless of the change in blood [illegible] of the heart decreases; [illegible] with disappearance of [illegible] waves become upright Patients may again feel well and lead normal lives. Those who had heart failure beforehand may manage without its recurrence. There is no change in renal function

Postural Effects

After lumbodorsal sympathectomy the blood pressure is highest when the patient is recumbent, it may be lower with the patient sitting up, and fall precipitously

to know what the operation implies. The object is to decrease peripheral resistance to the blood flow through a large portion of the vascular bed The earlier method (Adson, anterior rhizotomy) was a division of the anterior nerve roots of the spinal cord from the sixth dorsal to the second lumbar vertebral level, interrupting the sympathetic outflow to the splanchnic area This required extensive laminectomy and was too hazardous for wide use. Fall in blood pressure resulted with improvement in some cases This procedure was supplanted by a number of less formidable operations· cutting the sympathetic pathways above the diaphragm only (Peet), interruption below the diaphragm, and removal of the celiac ganglion.

Thoracolumbar Sympathectomy

The Smithwick procedure of thoracolumbar sympathectomy is perhaps the most widely used In this operation the complete ganglionated chain from the eighth thoracic to the third lumbar ganglia are removed, together with the greater, lesser, and least splanchnic nerves. Brain clips are attached to all of the divided ends to impede regeneration of the sympathetic chain. It is an extensive procedure and usually—unless it is undertaken in a very thin subject who is in excellent condition—the two stages are carried out at about seven- to ten-day intervals. In the exposure the lower ribs are resected and the diaphragm is usually divided. Intravenous pentothal induction followed by endotracheal ether and oxygen is the best anesthesia Positive pressure can be instituted if the pleura is entered. Usually, 5 per cent glucose is given intravenously during the first operation and citrated blood during the second Moderate fall in blood pressure may occur following the operation on one side but is most marked when completed on the second side Neosynephrine intramuscularly or intravenously has been used recently to counteract the precipitous fall in blood pressure, usually during the second stage of the operation Early ambulation is possible if there are no contraindications If pneumothorax occurs the air can be withdrawn by aspiration as the wound is closed.

Ray's result with lumbodorsal sympathectomy in 300 patients one to six years after operation will be summarized I have had the opportunity of seeing a number of these patients.

1 There were nine deaths, a mortality rate of 3 per cent.

2. In 10 per cent the blood pressure was unchanged or became higher.

3 In 16 5 per cent the blood pressure (both systolic and diastolic) fell to normal (to or below 140/95).

4 In 12 4 per cent the blood pressure fell but did not reach normal. It did not, however, exceed 150 mm. systolic or 100 mm diastolic.

5. In 31 6 per cent the blood pressure was reduced and the highest diastolic level postoperatively did not exceed 115 mm. The results in these patients were considered good

6 In 17.8 per cent there was significant reduction in both systolic and diastolic pressure while the diastolic pressure exceeded 115 mm. In these patients the results are considered fair.

If the results in (3) and (4) above are combined, one finds 28 9 per cent with a normal or near normal blood pressure; 31 6 per cent with a good result, and 17 8 with a fair result.

the fall in blood pressure has not always been maintained, the initial effect has been good, with clearing of the retinae, maintenance of compensation, and attainment of a moderate degree of activity within the limits of continued supervision and medication

The selection of patients for the operation, after the definite contraindications have been considered, should be based on the following factors. The subjects should be under 50 years of age with minimal eyeground changes and diastolic pressures less than 140 mm. Hg It may be expedient to waive on occasions certain of these requirements. The results are more favorable in women than in men. If nothing is known of the course and duration of the hypertension, the patient should be observed for several months to derive a notion of its variation and what can be accomplished by medical measures If there are no contraindications, the operation and the surgeon's and physician's opinions should be discussed with the patient, who alone makes the decision. The benefits cannot be so surely predicted that the patient should be urged to undergo the operation During the preliminary study all other causes of hypertension should be ruled out· pyelonephritis, unilateral kidney disease, coarctation of aorta, and pheochromocytoma may be mentioned

The following studies are made· x-ray of the heart, electrocardiogram, renal function as defined by the blood urea nitrogen, urea clearance, phenolsulfonphthalein excretion, dilution and concentration tests, intravenous pyelograms, and retrograde pyelograms if they are indicated. The lability of the blood pressure is observed. If the blood pressure is not fixed and declines during sleep, there is more reason to think that it will fall as a result of operation. The various tests which have been employed to prognosticate fall in blood pressure have not turned out to be of great value. Among these tests are the sedation or sleep test using amytal, the cold pressor test, the use of tetraethylammonium (Etamon), of priscoline, and of dibenamine.

The following facts should be kept in mind: A great number of patients have essential hypertension for many years and get on very well for the greater part of the time, symptoms and complications may become more serious with later years. At any rate the disease, untreated by sympathectomy, is of long duration. If we could be sure that complications and increasing disability would not be a cause of concern for many years, we would naturally hesitate to advise operation in the earlier stages of the disease. Unfortunately, this prediction cannot be made with any accuracy

Benefits Derived

The test of lasting benefit from surgery in these patients must be whether the course of the disease in the operated patient differs materially from that in the untreated patient These data are not available today. The statistics of the natural history of hypertension are sketchy and vary with the interest of those making the special survey. Even the incidence of hypertension in the whole population is not known Studies of large series of patients subjected to operation and observed for their whole life course are necessary, and it will be many years before these are accumulated

when the patient stands. Patients may therefore faint upon standing due to pooling of blood in the splanchnic area. Although this may be troublesome immediately after operation, patients learn within a few weeks or months to accommodate for it. A well-fitting belt or binder is used and should be adjusted with the patient lying down. Binding the feet and legs as far as the knees may be beneficial. When standing up the patients must learn to keep moving about slightly.

Other Effects

Patients may sweat excessively in the undenervated and upper part of the body in summer and feel cold in this area in winter. Coldness of the hands is a common postoperative complaint. This is due to compensatory vasoconstriction in the unsympathectomized parts of the body. Improvement occurs after a few months. Some patients develop Raynaud's phenomena without tissue changes. In two such patients removal of the remaining thoracic sympathetics including the stellate ganglion (total sympathectomy) gave relief. In men, section of the eighth dorsal to the third lumbar does not interfere with erection and orgasm but ejaculation may not occur. This can be obviated by preservation of one lumbar chain. The full benefits of operation may not be felt for six months. About a month's hospitalization is required for operation and mobilization. A period of two to four months should be planned for convalescence, which may be further delayed by adjustment to postural hypotension.

Ray has studied the *visceral sensation* after thoracolumbar sympathectomy. Sensation is lost in the gastrointestinal tract above the rectum, in the biliary and pancreatic systems, and in the upper urinary system. This is a source of potential hazard and must be kept in mind. It is fortunate that sensation to the parietal peritoneum is not affected so that nausea and vomiting, jaundice, abdominal distension, rigidity, tenderness on palpation, fever, and leukocytosis can occur. The gallbladder should be visualized before lumbodorsal sympathectomy. If stones are revealed the possibility of postoperative gallstone colic without pain should be kept in mind.

Selection of Patients for Operation

In general, patients with serious functional damage of the brain, heart, or kidneys should not be subjected to operation. Patients with acute encephalopathy should be excluded, but a history of strokes without other cerebral complications is no contraindication. Persistent nitrogen retention—with a blood nitrogen above 25 mg. per 100 cc.—low urea clearance, and fixation of specific gravity of urine are among the signs of decreased renal function which should be considered as contraindications to the operation. It is probably best not to operate on patients with glomerulonephritis.

Patients with myocardial infarction or a history of it should not be subjected to the operation, but angina may be relieved if the selection of patients for the operation is careful. Generally patients suffering from heart failure at the time of admission or in the past should be refused operation. However some patients have been restored to compensation with mercurial diuretics and digitalis and then subjected immediately to operation, using ether and intratracheal oxygen. Although

Postoperative Complications

1. When *pneumothorax* occurs, air can be removed by syringe before closure of the wound. The use of intratracheal ether and oxygen anesthesia allows expansion of the lungs when the pleura is opened

2. *Atelectasis* is treated in the usual manner, namely turning of the patient frequently, use of oxygen by tent or by mask, and the administration of penicillin to prevent pneumonitis. A mucus plug may require removal by suction.

3. *Pleural effusion* is removed by tap if it gives rise to respiratory or cardiac embarrassment.

4. *Cerebral thrombosis* may occur if there is marked fall in blood pressure, following the section on either the first or on the second side, especially in the presence of marked cerebral arteriosclerosis.

5. When the coronary vessels are the site of marked arteriosclerosis, *coronary thrombosis* may occur if there is considerable fall in blood pressure; or on the other hand myocardial infarction may occur without coronary occlusion.

6 Some patients experience *pain in the back* for many months after operation.

7. The *loss of ejaculatory function* in males if the section of $L_{2 \text{ and } 3}$ is included on both sides has been mentioned. In women there is no alteration in sexual function.

Bilateral Adrenalectomy

Bilateral adrenalectomy has been performed on a few patients suffering from severe hypertension This form of therapy is, however, in the experimental stage.

PREGNANCY AND HYPERTENSION

Many women with essential hypertension should be advised not to become pregnant (p. 489) Pregnancy under these circumstances is beset with complications for the mother and it may not be possible to secure a living child if the progress of the disease is accelerated or latent symptoms become manifest. When the patient is first seen after she is pregnant, if the blood pressure is not at alarming levels, if renal function is satisfactory, if there is no albuminuria, and if there are no eyeground changes, pregnancy may be allowed to continue but the progress is followed carefully Pregnancy may require termination by therapeutic abortion whenever there is any deterioration in the patient's status, either renal or cardiac.

Splanchnic Resection

Women who have had lumbodorsal splanchnicectomy for hypertension should be advised not to become pregnant even though the blood pressure has fallen to normal levels and remains there. We know too little about the course after this operation to foretell the natural history of the disease in such individuals. If a patient has a normal blood pressure after operation its stability should be the first concern.

On the other hand there has been some experience with patients who have become pregnant after lumbodorsal sympathectomy and there are even a few instances in which this operation was carried out early in pregnancy. This experi-

In the absence of statistical proof of the benefits of surgical treatment, the following represents an attempt to summarize our available knowledge:

There are no medications or procedures available at present except thoracolumbar sympathectomy which brings about so prolonged a *fall in blood pressure*. Those who use the argument that the blood pressure falls from any operation in which general anesthesia is used and that the rest in bed is the main factor are not being realistic.

Significant lowering of pressure should be beneficial, since it is the rise in blood pressure and the sustained elevation of diastolic pressure which increase the load *of the heart.*

Regression of the eyeground changes must be interpreted as a good omen. Ray has compared the natural history of the disease in the patients he has operated with the expected life span of patients who were unoperated. The patients were compared with a series of patients not subjected to operation reported by Keith, Wagener, and Barker and both series were classified according to the magnitude of the preoperative eyeground changes. In those with severe grades of eyeground changes, the number of patients surviving beyond the expected period was significantly greater than would have been predicted from Keith, Wagener, and Barker's data The mortality for the first year in those with Group III and IV eyeground changes was 14.2 per cent in Ray's series, compared with 69.4 per cent in the series of Keith, Wagener, and Barker This beneficial effect in prolonging life in the severer grades of hypertension is apparent. It is reasonable to assume that a comparable benefit might accrue in the less severe grades of hypertension.

If abnormalities regress in the eyegrounds—in a location in which direct observation can be made—it is in the realm of possibility that similar improvement may occur *in the cerebral, coronary, and renal vessels, although such changes do not* result in any improvement in renal function

Decrease in the size of the heart with the fall in blood pressure after operation must be regarded as a good sign. That decrease in cardiac size occurs with fall in blood pressure brought about by other means or on recovery from heart failure are not valid arguments against operative treatment.

It has already been pointed out that *decrease or disappearance of left axis deviation* may occur when the blood pressure falls after operation and the heart decreases in size. Such changes in axis deviation do not often occur spontaneously

Negativity of $T_{1,\,2,\,4}$ and *depression of* $RS\text{-}T_{1,\,2,\,4}$ generally appear and become accentuated as untreated hypertension progresses. These abnormalities are frequently removed by operation.

Patients with hypertension enjoy *relief of symptoms*, such as headaches, from the use of many of the measures employed in the medical management of the disease but the benefit is usually of short duration Patients whose symptoms—mainly headaches—are improved by sympathectomy on the other hand, may not have recurrence of those symptoms when there is a later rise in blood pressure Headaches are probably relieved by vasoconstriction of the extracranial arteries which are in the unsympathectomized region (Ray). The extensive experience provided by Dr. Dana W. Atchley's clinic at the Columbia-Presbyterian Medical Center *may* supply the control experience against which the results of surgical treatment may be gauged.

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ence has shown that these patients may go through pregnancy without any overt complications, without any apparent alteration of the functional (renal and cardiac) capacities, and without any or at most only temporary rises in blood pressure which return to near the pre-pregnancy levels afterward. Therapeutic abortion should be carried out if it is indicated by any changes in status.

SUMMARY

Hypertension occurs in a wide variety of diseases and has many causes. The most common type—so-called essential hypertension—is of unknown etiology. In its earliest stages the heart, brain, and kidneys are normal and functional and anatomic changes cannot be detected, but many forms of cardiac, renal, and cerebral damage are encountered in patients after the age of 30. Secondary hypertension, if allowed to become chronic, may lead to the same handicaps

The consequences of hypertension are due in part to the burden which it places on the heart, in part to arteriosclerotic changes which follow in its course; and in part to a combination of the two. The heart may fail because of the hypertension or because of the high blood pressure together with the arteriosclerotic changes in the coronary vessels. Alterations in the coronary circulation may cause angina and if the integrity of the vessels is greatly handicapped coronary thrombosis with myocardial infarction may result With either of these heart failure and various cardiac irregularities may occur.

Because of the cardiac, renal, and cerebral changes attempts have been made to lower the blood pressure In certain instances a low salt diet may be beneficial. The rice diet has been the most spectacular of the salt-poor diets to be used for this purpose. For the most part drugs have not been successful in lowering blood pressure over long periods of time. The most successful and most widely used procedure has been lumbodorsal sympathectomy according to the Smithwick procedure This is effective in a large enough percentage of patients with essential hypertension even after the onset of cardiac impairment to warrant the consideration of this operation for every patient with essential hypertension.

The management of patients with hypertension—including those patients who exhibit decline in blood pressure following sympathectomy—includes establishment of moderate ways of living, the use of the psychosomatic approach, and often more intensive psychotherapy by a trained psychiatrist. The after-results of hypertension run a wide gamut of medical and surgical complications, and require all of the art and skill of the practice of medicine.

There is nothing that can be done in the light of today's knowledge to prevent the occurrence of essential hypertension. Its full development and consequences may be delayed in those persons who exhibit transient rises in blood pressure in their earlier years by guiding the selection of life activities and work and instructing these patients in the effects of emotion, stresses, and strain on the development of this disease

CHAPTER 10

Hypotension

FORMS OF HYPOTENSION

Hypotension is said to be present when the systolic blood pressure is below 100 mm Hg Chronic hypotension may be a part of the clinical picture of diseases such as myxedema, Addison's disease, valvular heart disease when the lesion of aortic stenosis predominates, and chronic constrictive pericarditis, malnutrition, neurocirculatory asthenia, and psychoneuroses Fall in blood pressure also occurs in shock from any cause, in paroxysmal tachycardias when the heart rate is rapid, lusion, and in carotid lead to fainting essential" hypotension. In these persons the normal or low blood pressure falls to extremely low levels when the patient stands

Many patients with hypotension remain in good health and are without symptoms Many of the subjects with low blood pressure without any associated disease are thin, slim, lean individuals and not of the athletic type On the whole, low blood pressure favors longevity. Patients should not be told they have "too low blood pressure" They may then come to have as many symptoms as patients who have hypertension since they will often develop a fixation on the low blood pressure I do not recommend medications or other measures to raise the blood pressure of such patients In some patients chronic fatigue will be found together with low blood pressure In these cases the hypotension is not a cause of the symptoms, but is a part of the whole clinical picture which should be treated instead of the blood pressure per se. Too often we see patients treated for "low blood pressure" whose whole state of well being depends on whether they are told the blood pressure is 5 to 10 mm higher

When there is sudden fall in blood pressure (as with hemorrhage), the under-

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lying condition responsible for this is treated. The blood pressure usually rises in the course of recovery. Unless the blood pressure level is restored there may be pathologic changes in brain tissue. Moreover, changes in the myocardium attributed to infarction without closure of a vessel may be of adequate proportions to give rise to alterations in the electrocardiogram. In chronic low blood pressure associated with certain diseases such as Addison's disease and myxedema the blood pressure usually rises with correction of the primary underlying condition.

The cause of spontaneous postural hypotension is not known. Discussion has centered on whether it arises from a central or a peripheral mechanism Stead and Ebert think it is a disease of the sympathetic nervous system. They failed to detect vasoconstriction with fall in blood pressure. Postural hypotension implies a failure of the cardiovascular mechanism to adjust to changes in body position. In normal subjects the systolic blood pressure falls only slightly and the diastolic pressure rises slightly on changing from the supine to the upright position. When the subject with orthostatic hypotension stands, however, both the systolic and diastolic blood pressure fall, the patient becomes weak and feels faint, and syncope may occur Fall in blood pressure associated with faintness and with other symptoms occurs in many patients after splanchnic resection for the relief of hypertension, because of pooling of blood in the splanchnic bed when the patient stands. These symptoms and signs are minimized if the patient wears a tight abdominal binder and moves around while on foot (Chapter 9).

TREATMENT

It is very difficult to give any measure of relief to patients exhibiting spontaneous postural hypotension Some are benefited by wearing an abdominal binder, although undue pooling of blood in the splanchnic area in these subjects may not be demonstrated. Ephedrine 25 to 50 mg, amphetamine sulfate 5 to 10 mg, or paredrinol 20 mg. several times a day may be beneficial. Desoxycorticosterone and sodium chloride have been used with benefit in one patient Size of the heart, increase in weight as evidence of water retention, and rise in blood pressure should be carefully observed during this medication. Neosynephrine hydrochloride in 50-mg doses may be effective but may need to be repeated every two hours. Epinephrine in oil, 0.4 cc. intramuscularly, may give relief for several hours; massaging the area of the intramuscular injection when the effect is wearing off may give an added period of relief.

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lesions, or finally, whether arteriosclerotic lesions arise from synthesis of chemical substances in the body having no relation to the ingested cholesterol and result from an altered metabolism of the cells. It is probable that atheroma develops only when the ratio of cholesterol to phospholipid exceeds a certain level The dispersion of cholesterol is important. Phospholipids have the property of increasing the amount of cholesterol which will stay in solution; there are agents which alter this ratio. The reduction in oxygen consumption with advancing years together with abnormalities in fat metabolism may be factors which give rise to disturbance of the colloidal balance and allow deposition of fat in the intima of arteries. The clinical association of arteriosclerosis with myxedema in man and the development of arteriosclerosis with the depression of thyroid activity in dogs by thiouracil are probably related to changes in oxygen metabolism and not to the implication of the thyroid gland in arteriosclerosis.

Gofman has demonstrated the occurrence of increased serum levels of S_f 12–20 and S_f 35–100 lipoproteins in patients with arteriosclerosis, regardless of the age and total serum cholesterol level (S_f 12–20 means that the lipoprotein separated with the ultracentrifuge has a flotation rate of 12–20 Svedberg flotation units.) The S_f 12–20 level in the blood is stable and not acutely influenced by diet, although depression of high S_f 12–20 levels by restriction of fat and cholesterol has been achieved The S_f 35–100 level varies acutely with the diet.

Gofman regards the S_f 12–100 lipoproteins as the "atherosclerogenic band" of the lipoproteins He has found that the intravenous administration of heparin causes marked reorientation in the distribution of low density lipoproteins, characterized by a shift of lipoproteins of high S_f rates to those of successively lower S_f rates While Gofman has been able to demonstrate certain β-lipoproteins in increased amounts in the presence of arteriosclerosis, Barr has shown a diminished percentage and concentration of α-lipoproteins, indicating a defect in lipid metabolism in this disease and the possibility of dietary correction.

Treatment of Arteriosclerosis

Among recommended forms of therapy for the control of arteriosclerosis have been: (1) restriction of the caloric and fat intake in patients who are overweight or have elevated serum cholesterol levels, (2) promotion of oxidative processes by a high protein diet, by the use of oxytropic members of the vitamin B complex (nicotinic acid, thiamine, riboflavin), and thyroid extract, (3) the administration *of the lipotropic components of the vitamin B complex (choline, inositol, pyridoxine)*, and (4) stabilization of the plasma cholesterol by colloidal stabilizers such as lecithin and albumin.

A large percentage of patients with arteriosclerosis of the coronary arteries exhibit increase in the cholesterol content of the blood The significance of this finding is not readily apparent but from a practical standpoint it does not appear wise at the present time to alter the normal diet in an attempt either to prevent
sclerosis or to halt its progression unless the

CHAPTER 11

Arteriosclerotic Heart Disease

ARTERIOSCLEROSIS

Arteriosclerotic changes of the arteries of the coronary tree and of the valves of the heart may cause cardiac disease. These changes may be due to age, or they may occur earlier as a consequence of hypertension or of metabolic faults The signs and symptoms may result from (1) sudden decrease in or obstruction to the coronary circulation which in turn affects the functional capacity of the myocardium; (2) slowly progressive reduction in the coronary circulation resulting in chronic changes in the myocardium which affects its functional capacity; (3) anatomic deformity of the valves, especially the aortic one; and finally (4) a combination of these factors. The frequently concurrent hypertension may or may not have caused the arteriosclerosis.

In certain persons arteriosclerotic changes of the heart and blood vessels appear early, as if the patient were predisposed to this abnormality. Others may suffer from xanthomatosis. The changes may fit into a pattern known as "essential familial hypercholesterolemia." In younger persons *Monckeberg's sclerosis* of the valves may be the cause of valvular deformity.

The observations of Wilens relative to the appearance of arteriosclerosis are of interest There is at necropsy a high incidence of severe atherosclerosis in obese persons, while severe or even moderate atherosclerotic changes are seldom found in persons who have been subjected to protracted malnutrition. Moreover, less severe changes are observed in patients with wasting diseases than in those with terminal weight loss. He makes the inference that significant resorption of atheromatous lesions may occur during periods of marked weight loss. The early lesions are more susceptible to regression than the later ones.

We have no means to prevent arteriosclerosis. It is not known in man whether ingested cholesterol is directly transferred to the formation of arteriosclerotic lesions, whether it is metabolized and utilized as building stones for arteriosclerotic

out the coronary tree. On other occasions small localized areas of arteriosclerosis may be the site of thrombosis even in young individuals. Coronary artery disease may cause fibrotic changes in the myocardium as a result of diffuse ischemia, without actual closure of coronary vessels. Arteriosclerotic changes of the coronary arteries predispose to coronary thrombosis, resulting in myocardial infarction due to interruption of the blood supply. Heart failure may result from the disease.

Varying grades of heart block up to complete heart block as well as bundle branch block may result from decline or interruption of the coronary circulation to the septal region.

Xanthomatosis may involve the coronary arteries and be the cause of angina—particularly in young patients—or of myocardial infarction. Hypercholesterolemia should also be considered.

Myocardial Fibrosis or Myocardial Disease

Generalized myocardial fibrosis results from diffuse narrowing of the coronary vessels by arteriosclerosis, with or without hypertension. Localized areas of fibrosis may also result from previous myocardial infarctions. Ventricular premature contractions are a common occurrence in older individuals with myocardial damage and may require therapy per se if they cause discomfort. Auricular fibrillation is less common than in those exhibiting rheumatic mitral stenosis. Electrocardiograms may show low amplitude of the QRS complexes with slight left axis deviation. Alterations of the T waves and RS-T segments indicate concurrent coronary artery disease. There may be all grades of heart block up to complete auriculoventricular dissociation as well as bundle branch block when the conduction system is involved in scar tissue. The heart may be enlarged, although some believe that this only occurs in patients with a history of hypertension.

Cardiac arrhythmias and heart failure are treated in the usual manner.

Arteriosclerosis of Pulmonary Arteries

This manifestation is discussed in Chapter 16, relating to chronic cor pulmonale.

Arteriosclerosis of Aorta

Arteriosclerotic changes of the aorta are common as aging phenomena and as a consequence of hypertension Calcified plaques may be seen in the arch of the aorta in roentgenograms of the chest A systolic murmur may be heard over the base of the heart In most instances arteriosclerotic changes of the aorta give rise to no embarrassment of the heart per se except in so far as the general loss of elasticity and hardening of the vascular tree alter the dynamics of the circulation. Even in instances proceeding to formation of aneurysms of the aorta, the function of the heart is not impaired unless the valves and coronary arteries are also compromised

AGING HEART MUSCLE

Either natural or accelerated aging of heart muscle in the presence of an apparently adequate coronary circulation—when restriction of its blood supply by arteriosclerotic changes cannot be demonstrated—may be a cause of cardiac enlarge-

Restrictions to an effective degree do not provide an "adequate" diet. Choline and inositol have not influenced the development of arteriosclerosis in animals. Patients with high serum cholesterol may be given a low fat, low cholesterol diet without out being certain that the course will be altered favorably. There is not good evidence that vitamin E has any effect on the arteriosclerotic process or on the resulting symptoms. A long-term controlled study in manipulation of the diet may be of significance but to change the dietary pattern of isolated patients without provision for such a study does not at present appear warranted. The avoidance of eating too many calories, too much fat, and perhaps, too much cholesterol, and of obesity in all adult individuals, is, at present, the best safeguard against the development of arteriosclerosis.

Cardiac Manifestations

Arteriosclerosis may affect several parts of the heart and the great vessels.

Arteriosclerosis of Aortic and Mitral Valves

PATHOLOGY. Changes in the valves of the heart with or without hypertension occur at an earlier age in some individuals than in others The valve leaflets become stiff and thickened and at various stages may exhibit all the typical changes of arteriosclerosis with calcification of the valves. The mitral and aortic valves are most commonly affected. There may be signs of mitral insufficiency and aortic "roughening." As changes in the aortic valve become more marked, this may develop into aortic stenosis, so-called *calcific aortic stenosis* with or without clinical evidence of aortic insufficiency and with marked dyspnea, angina, and syncope. Less rarely there may be mitral stenosis The stigmata of rheumatic infection have been found at autopsy in many cases of calcific aortic stenosis and of mitral stenosis even though there may have been no previous evidence of this disease The calcified, narrow aortic orifice obstructs the egress of blood from the heart and thereby increases the burden on the left ventricle. The left ventricle hypertrophies and cardiac enlargement extends to the left Calcification of the valve may be seen in spot x-ray films of the heart.

In addition to calcific aortic stenosis there may be also *narrowing of the coronary arteries* which may cause a great exaggeration of the effects of the stenosis. Patients exhibiting calcific valvular disease are subject to subacute bacterial endocarditis, a diagnosis which is frequently overlooked as a cause of fatigue and low-grade fever in older individuals

TREATMENT. Patients are urged to live at a slow pace, to walk slowly, and to rest frequently in order to avoid overburdening the heart Angina, heart failure, and subacute bacterial endocarditis are treated in the usual fashion when they occur Events which induce syncope should be avoided.

Arteriosclerosis of Coronary Arteries

Arteriosclerotic changes in the coronary arteries, so-called *coronary artery disease*, may be present without giving rise to symptoms or to changes in the functional capacity of the heart. When symptoms are present, the most common is angina pectoris This subject is discussed in Chapter 12 (angina), and in Chapter 13 (coronary thrombosis). The arteriosclerotic changes are usually scattered through-

out the coronary tree. On other occasions small localized areas of arteriosclerosis may be the site of thrombosis even in young individuals. Coronary artery disease may cause fibrotic changes in the myocardium as a result of diffuse ischemia, without actual closure of coronary vessels Arteriosclerotic changes of the coronary arteries predispose to coronary thrombosis, resulting in myocardial infarction due to interruption of the blood supply. Heart failure may result from the disease.

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AGING HEART MUSCLE

Either natural or accelerated aging of heart muscle in the presence of an apparently adequate coronary circulation—when restriction of its blood supply by arteriosclerotic changes cannot be demonstrated—may be a cause of cardiac enlarge-

ment, decline in the functional capacity of the heart, and heart failure. This etiologic diagnosis during life is arrived at by exclusion. Although aging may be a factor in the occurrence of heart failure in most older individuals—and as I have indicated on occasion it may be the only etiologic factor which can be postulated—anatomic changes in the coronary vessels are usually the predominating ones.

Treatment

Means are not available of altering the course of the deterioration of the cardiac muscle.

The treatment of the congestive manifestations is the same as in other instances of heart failure.

SUMMARY

Arteriosclerotic heart disease is the commonest form of heart disease in older individuals. All parts of the heart may be affected by the arteriosclerotic process: the coronary arteries, the heart muscle, the valves, and the aorta. Involvement of these may give rise to appropriate symptoms and signs which may require therapy. It may be recalled that arteriosclerotic changes in the vessels of other major systems, namely the kidneys, the brain, and the peripheral vascular tree, are also the cause of alterations of function of these systems.

The train of events leading to the initiation of arteriosclerotic changes is not known. Nor do we have clinical means for the prevention of arteriosclerosis, for halting its progress, or for reversal of the changes once they have taken place. The extensive interest in the so-called degenerative diseases should, however, give encouragement that an understanding of the nature of arteriosclerosis may be arrived at, an achievement which will be expected to lead to the institution of appropriate therapeutic measures for delaying its progress or for alleviating its consequences.

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Precordial pain is an expression of impairment in the function of the coronary circulation which results in ischemia, a consequence of a change either in quality or in quantity of the blood delivered to the myocardium. The most common cause of alteration in the amount of blood transferred to the mass of cardiac muscle is arteriosclerosis of the coronary arteries. This may be generalized or the total coronary bed may show minimal alterations with marked localized changes The lumens may be intact but diminished in cross section. On the other hand a vessel may be completely occluded by thrombus formation, by hemorrhage within the arteriosclerotic wall so that there is a bulge into the lumen, or by an embolus, matters which are discussed in Chapter 13. The coronary circulation may be impaired, even though the coronary vessels are normal, should the blood pressure fall as in shock, in aortic insufficiency, because of the sharp fall in diastolic pressure with a wide pulse pressure, in mitral stenosis, in aortic stenosis, in paroxysmal tachycardia, in hyperthyroidism, in syphilitic aortitis with involvement of the coronary ostia, and in emotional states. In any of these situations ischemia may more easily result if there is concurrent anemia.

The term coronary insufficiency has been used to describe the state of ischemia of the heart muscle which results from impairment of its blood supply It may be looked upon as a discrepancy between the requirements of the heart muscle for blood and the amount which it receives Various degrees of coronary insufficiency give rise to different signs and symptoms At one end of the scale is myocardial ischemia which is transient and may be associated with angina and transient electrocardiographic changes. At the other end of the scale is more prolonged and persistent ischemia which gives rise to necrosis of heart muscle—namely myocardial infarction. The amount of blood supplied the heart muscle may be adequate at rest or moderate exertion but is inadequate for (1) more marked exertion, (2) exertion which is undertaken after eating when the blood is pooled in the splanchnic area; (3) exertion which is engaged in when there is vasoconstriction due to exposure to cold or associated with emotion, (4) exertion when the patient is anemic and the oxygen-carrying capacity of the blood is compromised, (5) occasions when there is fall in blood pressure

Angina is more common in men than in women

SYMPTOMS

Pain on effort is the characteristic feature of angina pectoris, although pain may be associated only with emotional distress. Some patients suffer angina only when exerting themselves in a particular manner, as, for instance, if they exercise after eating and when exposed to cold or when walking against the wind

The *typical pain* which Heberden described as angina pectoris was localized in the precordial area, in the pectoral region, with radiation down the left arm There

may be felt by the patient in the substernal region on the right and in some cases is isolated there.

CHAPTER 12

Coronary Artery Disease and Angina Pectoris

Arteriosclerosis of the coronary arteries, commonly known as coronary artery disease, brings about narrowing of the lumens of these vessels. The intimal changes may progress to the formation of atheromatous lesions. Arteriosclerosis is looked upon as evidence of aging of the vascular system, but the changes occur early in some individuals and later in others. Experience in World War II demonstrated an incidence greater than earlier statistics had indicated of coronary artery disease in subjects in the draft age group The pathogenesis of arteriosclerosis is being given a great deal of attention at the present time, but the events leading to alteration in the vessels are not at present known. In what way disturbance in lipid metabolism and more especially aberration of the cholesterol metabolism leads to atheroma is at present a matter of conjecture. Heredity appears to be a potent factor. Hypertension may be the forerunner. In young individuals coronary artery disease may be occasioned by xanthomatosis associated with hypercholesterolemia. Coronary artery disease may be advanced in patients with diabetes.

Coronary arteriosclerosis may be present without giving rise to signs and symptoms. In certain patients it may give rise to the symptom complex known as angina pectoris; in others it may be the basis for coronary thrombosis, or for congestive heart failure. The various clinical manifestations of coronary artery disease are shown in Fig. 37.

Angina pectoris is one of the most common manifestations of these pathologic changes in the coronary arteries. Angina pectoris is a syndrome characterized by pain in the pectoral muscle region, radiating down the left arm, brought on by effort and relieved by resting or nitroglycerin. The symptom is also known as "angina of effort," "pain on effort," and "coronary insufficiency." Angina is a symptom complex and not a disease entity, since it is associated most frequently with coronary artery disease, it has loosely come to be synonymous with it.

graphic alterations, or may not give evidence of either reaction. A positive response of either or both types—electrocardiographic changes or pain—is presumptive evidence of coronary insufficiency but electrocardiographic changes are more significant. Levy has set up criteria for the quantitative aspects of the electro-

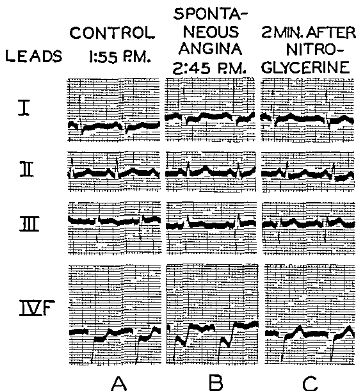


FIG 38

Electrocardiograms Taken During Spontaneous Angina Pectoris and Immediately Afterward, Following Use of Nitroglycerin Electrocardiograms relate to a man 59 years of age who had severe angina pectoris

A, serving as control, was taken at 1 55 P M Its most significant abnormality was depression of $RS\text{-}T_4$

...-T_1 and

...t relief

...gram to

control configuration

cardiographic changes. Qualitatively, they consist of a trend towards negativity and segmental depressions in the T waves and RS-T segments. They are promptly dissipated by breathing 100 per cent oxygen.

Certain precautions and contraindications to the test should be remembered: Patients with past or present heart failure or with a history of myocardial infarction within the past six months should not be given the test. Pulmonary disease, mitral stenosis, anemia, myxedema, and pregnancy are also contraindications. The test

The most frequent *referral of pain* is to the left arm; it may be to the shoulder, to the inner side of the arm, the elbow, the wrist, or even to the thumb or the fingers. The symptoms of such referred pain may be described as "severe pain," as "numbness and tingling" or as a "cramplike pain." Less frequently pain is referred to the right arm, rarely without any reference to the left arm. Patients may have only substernal distribution of discomfort with moderate attacks, referral of distress to the left arm with more severe attacks, and to the right arm with the most severe attacks. Pain may also be referred to the throat, the neck, the angle of the lower jaw, the teeth, and even the occiput. Instances are recorded of the referral of cardiac pain to *phantom left arms.*

Patients may sweat profusely during an attack of pain and have a sense of impending death. In typical cases the pain which has appeared upon exertion passes promptly if the patient stops and rests or if the patient dissolves a nitroglycerin tablet under the tongue During precordial distress patients may experience *hyperesthesia of the anterior chest wall, so that the clothing causes unpleasant* sensations: the so-called "Head's zones of hyperalgesia."

Angina lasts from one to five minutes and rarely persists 15 minutes or longer. *Persistence of pain for longer periods suggests more marked ischemia resulting in* myocardial infarction. The frequency of attacks varies They may occur at infrequent intervals of several weeks or recur many times daily depending upon the avoidance of precipitating factors and the optimal use of available medication.

DIAGNOSIS

In the diagnosis of angina pectoris the clinical history is the most important part of the examination While the subjective symptoms may be typical of angina pectoris, physical examination may reveal no abnormal features relating to the cardiovascular system. The blood pressure, the size of the heart, and the electrocardiographic tracings may all be normal—in short, there may be no objective signs of coronary artery disease. Vascular changes in other parts of the body, namely *in the peripheral vessels, in the aorta, in the eyegrounds, and in the kidneys* when there is decreased renal function, would make it easier to infer that changes in the coronary arteries may also be present. In most patients, however, the presence of *arterial hypertension, cardiac enlargement, abnormal physical signs of the heart,* and electrocardiographic abnormalities give *objectivity to the patient's symptoms* When the pain is atypical and the objective evidence of coronary artery disease is lacking certain tests have been devised to provide objective records which are interpreted in terms of changes in the coronary circulation. They are as follows:

Anoxemia (Hypoxemia) Test

The patient breathes a mixture of 10 per cent oxygen and 90 per cent nitrogen while serial electrocardiograms are taken for comparison with a control. Normal subjects exhibit no significant changes in their electrocardiograms and do not experience *precordial pain after breathing this mixture for 20 minutes.* Subjects in whom the coronary circulation is impaired may experience pain alone or exhibit electrocardiographic changes alone, may both suffer pain and show electrocardio-

Significant changes in the T waves and RS-T segments after exercise are observed in many patients with typical clinical angina. The inference is made that significant changes after exercise give objective evidence of coronary insufficiency. Proceeding one step further, a positive electrocardiographic exercise test may be used as evidence of angina in instances when the pain is not typical. A physician should be present when this test is being done in order to gauge the effect of the exercise and to discontinue the test should further exercise appear unwarranted. Care must be exercised that acute pulmonary edema does not occur A second resting electrocardiogram is taken 20 minutes after exercise to discover whether the changes in the tracing have disappeared. The patient is kept at rest until this occurs. Patients may experience bundle branch block during the exertion and changes may persist for several hours

Electrocardiographic Changes During Spontaneous Angina

During the occurrence of spontaneous angina pectoris, transient electrocardiographic alterations may be recorded which are similar to those induced during anoxemia and exercise tests Nitroglycerin may bring about a rapid reversal of the electrocardiogram to its control contour in spontaneous angina (Fig. 38) but may be slower in inducing its effects after exercise (Fig 39).

The Ballistocardiograph

Abnormalities of the form of the ballistocardiographic pattern have been observed in coronary artery disease In certain instances the usual waves cannot be identified As correlations are substantiated the field of usefulness of this technic may be more clearly defined.

Other Tests

The vasoconstrictor effects of epinephrine or of pitressin should not be used to induce pain in order to acquire evidence of coronary insufficiency. It does not appear safe to use drugs which raise the blood pressure for this purpose I have had no experience with the use of ergonovine maleate as a test of coronary insufficiency It is used in 0 2-mg amounts intravenously and is said to induce electrocardiographic changes similar to those of the anoxemia test

Differential Diagnosis

Cervical Rib and Scalenus Anticus Syndromes

Cervical rib and scalenus anticus syndromes may cause pain in the left arm which mimics the distribution of angina pectoris In both these syndromes sensory changes in the arm may be detected as well as alteration in the blood pressure and in the volume of the radial pulse The cervical rib may be revealed by roentgenograms

Hiatus Hernia

In some instances the symptoms associated with hiatus hernia may be confused with those of angina pectoris Special fluoroscopic and x-ray technics must be carried out by those experienced in tracking down this abnormality. It may require several examinations before visualization of the hiatus hernia is successfully ac-

should not be repeated within twenty-four hours and it would be wise to compare the control electrocardiographic tracing with previous ones—if available—to ascertain whether *any recent subclinical myocardial damage has occurred.*

The use of ergotamine 0.5 mg. intramuscularly or subcutaneously 20 minutes before the anoxemia test does not appear to be a useful procedure although I

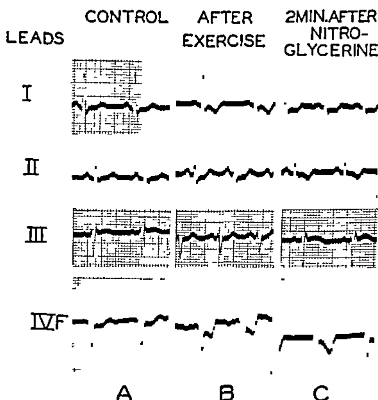


Fig. 39.

Electrocardiograms Taken as a Part of an Exercise Test, Showing Effect of Nitroglycerin These electrocardiograms were derived from patient described in Fig 38

more marked

more because

ve test. T_1 be-

and changed

form, and RS-$T_{1,\,2,\,\text{and}\,4}$ became more depressed Two minutes after administration of nitroglycerin pain had disappeared

C, taken at this point, showed further changes but had not returned to its control configuration

have had no experience with its use. It is claimed that ergotamine blocks the sympathetics and eliminates reflex emotional or functional factors which might produce false positive results (Biorck).

Exercise Test

In this test electrocardiograms taken after exercise are compared with control resting records. The patient may walk over steps until dyspnea or pain occur. I do not enforce any set speed or any prescribed number of turns over the steps.

I usually ask what reason has been assigned for their symptoms by other physicians in order to discover what medical terms may be known to them. I try to explain to patients in simple terms the role of the coronary arteries in the blood supply of the heart muscle and its need for an increased amount of blood during exertion I explain that the nearest the heart can approach to complete rest is when the patient is in the basal state; that any exertion over this basal work makes the heart work harder. Then I discuss the effect of aging on narrowing of the lumens of the coronary vessels, resulting in decrease in amount of blood supplied to the heart muscle. I explain that the coronary flow may be adequate during rest or moderate exertion, but that it is insufficient for much exertion, or for exertion under special circumstances. I tell the patient that the expression of the inadequacy of the coronary circulation is pain, or whatever other symptoms this patient has. I do not mention any symptoms the patient does not have I finally label the disease to the patient as pain on effort or exertion or perhaps inadequacy or insufficiency of the coronary circulation. If the patient is familiar with the term "angina pectoris" he is reassured that it means "pain in the breast or chest area." Emphasis is placed *upon the idea that understanding the mechanism of his symptoms is the important thing*, for by this means he will acquire insight which will aid in his own regulation of activities. A careful history should give the physician the background for setting up the patient's regimen. It may be necessary before outlining the patient's plan of therapy to inquire into the details of the patient's activities more closely than was done in taking the original history

General Activities

The general activities which precipitate attacks should be analyzed in order to discover if these can either be carried out more leisurely or even omitted The patient is advised to learn to do things slowly. He should walk slowly, use elevators when they are available, climb stairs slowly when they cannot be avoided, resting after every few steps. If symptoms appear when walking along the street, patients can acquire the habit of looking in shop windows while they rest in order not to appear conspicuous They are advised to stop immediately when symptoms appear, and not to try to continue the exercise

Daily Routine

The daily routine is analyzed in order to ascertain what is wise for the patient to continue and what should be eliminated Executives may find it beneficial to rest after lunch Business should be avoided at lunch time. Events that lead to emotional tension and pain should be avoided. Some patients may find it necessary to change the work they are doing if it is not congenial and if it gives rise to mental or exertional distress Other patients may be able to shift to other work in their organization when the help of supervisory officers is enlisted

Exercise

Exercise should be avoided after eating, when this cannot be done, exertion should be undertaken with caution Attacks of angina are more easily precipitated after eating because of abdominal distention and pooling of blood in the splanchnic area.

complished. In some instances when hiatus hernia is suspected but the roentgenologist has not been successful in demonstrating it, patients may be placed on small, frequent feedings and tincture of belladonna administered before each meal in order to make a therapeutic test. This regimen may give relief to patients with hiatus hernia, but would not be expected to be of benefit in the presence of angina

Spontaneous Mediastinal Emphysema

Symptoms associated with spontaneous mediastinal emphysema are more likely to simulate those of myocardial infarction than those of angina. Its occurrence in young individuals, the typical crunching substernal sound, the absence of electrocardiographic changes (although this is not always the case), and detection of air *under the sternum or in a pleural cavity in roentgenograms usually makes the* diagnosis of this lesion certain.

Cervical Disc

In certain instances the symptoms due to a cervical disc or cervical nucleus polyposus have simulated those of angina.

Gallbladder Disease

Occasionally gallbladder disease may give symptoms which may be confused with those of angina pectoris. On occasion, when gallstones are visualized in patients in the coronary artery disease age group or when the gallbladder cannot be visualized, it may be difficult to establish which components of the symptoms may be due to gallbladder disease and which ones are to be attributed to coronary artery disease. It is in these instances that the anoxemia or the exercise test may be of help in differential diagnosis

Patients with *porphyria* may have precordial distress. It may occur at rest There may be nonspecific changes in the electrocardiogram.

TREATMENT

There are two objectives in the treatment of angina:

1 To terminate as quickly as possible and to reduce the severity of individual attacks. Most attacks—especially those associated with exertion—are of short duration and are relieved promptly when the patient rests Other attacks require medication to insure prompt relief.

2. To reduce the frequency and severity of attacks. Much of the therapeutic regimen is directed toward this end In addition the underlying disease should be accorded whatever treatment is available and contributory factors should be eliminated—syphilis, hypothyroidism, hyperthyroidism, diabetes, gallbladder disease, and anemia, to mention a few.

General Management

Orientation of Patient

I do not use the term "angina pectoris" in discussing the disease with patients unless they have already been given this diagnosis and are familiar with this term.

I usually ask what reason has been assigned for their symptoms by other physicians in order to discover what medical terms may be known to them. I try to explain to patients in simple terms the role of the coronary arteries in the blood supply of the heart muscle and its need for an increased amount of blood during exertion. I explain that the nearest the heart can approach to complete rest is when the patient is in the basal state, that any exertion over this basal work makes the heart work harder. Then I discuss the effect of aging on narrowing of the lumens of the coronary vessels, resulting in decrease in amount of blood supplied to the heart muscle. I explain that the coronary flow may be adequate during rest or moderate exertion, but that it is insufficient for much exertion, or for exertion under special circumstances. I tell the patient that the expression of the inadequacy of the coronary circulation is pain, or whatever other symptoms this patient has. I do not mention any symptoms the patient does not have. I finally label the disease to the patient as pain on effort or exertion or perhaps inadequacy or insufficiency of the coronary circulation. If the patient is familiar with the term "angina pectoris" he is reassured that it means "pain in the breast or chest area" Emphasis is placed upon the idea that understanding the mechanism of his symptoms is the important thing, for by this means he will acquire insight which will aid in his own regulation of activities. A careful history should give the physician the background for setting up the patient's regimen. It may be necessary before outlining the patient's plan of therapy to inquire into the details of the patient's activities more closely than was done in taking the original history

General Activities

The general activities which precipitate attacks should be analyzed in order to discover if these can either be carried out more leisurely or even omitted The patient is advised to learn to do things slowly. He should walk slowly, use elevators when they are available, climb stairs slowly when they cannot be avoided, resting after every few steps. If symptoms appear when walking along the street, patients can acquire the habit of looking in shop windows while they rest in order not to appear conspicuous They are advised to stop immediately when symptoms appear, and not to try to continue the exercise

Daily Routine

The daily routine is analyzed in order to ascertain what is wise for the patient to continue and what should be eliminated Executives may find it beneficial to rest after lunch. Business should be avoided at lunch time Events that lead to emotional tension and pain should be avoided Some patients may find it necessary to change the work they are doing if it is not congenial and if it gives rise to mental or exertional distress Other patients may be able to shift to other work in their organization when the help of supervisory officers is enlisted

Exercise

Exercise should be avoided after eating, when this cannot be done, exertion should be undertaken with caution. Attacks of angina are more easily precipitated after eating because of abdominal distention and pooling of blood in the splanchnic area.

Cold Weather

The patient should walk more slowly in cold weather. Walking should be avoided whenever possible if exposure to cold is a precipitating factor. Some patients may find it possible to go to a warm, dry climate for the winter months.

Management of Weight

If the patient is overweight reduction in weight is indicated. Frequently this can be managed by the restriction of starchy foods and fats, without the complete elimination of any articles of food. For example, a small potato might be allowed instead of a large one and bread limited to one slice of toast for breakfast. Fresh or stewed fruits without sugar are useful for desserts. The data relating to the association between high cholesterol diets and clinical atherosclerosis are not precise enough to warrant drastic manipulation of the diet.

Abdominal Binder

I have had no particular success with the use of an abdominal supporter for the prevention of attacks of angina. An abdominal binder may be tried before putting the patient to the expense of having an abdominal support made.

Bed Rest

Complete bed rest is only occasionally indicated in the treatment of angina pectoris If the pain is such that the question of coronary thrombosis or of rapid or progressive closure of a vessel arises, the patient should remain at rest in bed until this possibility is eliminated A patient may be having attacks so frequently and may be working under such conditions that only rest in bed can break the cycle and provide needed rest. In most of the other cases strict bed rest is not indicated but only restriction of activity to the degree that is compatible with comfort Rest from all but minimal exertion may be required in some patients. In other patients relief from their usual responsibilities may have a beneficial effect on the symptoms and allow the development of a collateral circulation which will serve in good stead later.

There are occasions when patients have premonitory attacks of pain without any electrocardiographic changes for a week or ten days before the occurrence of coronary thrombosis, which can be recognized by the occurrence of severe pain, fall in blood pressure, and other manifestations of myocardial infarction. If these patients could be sifted out and put to rest in bed, a less severe after-course might result, but there appears to be no way at present of identifying these patients with certainty.

Smoking

Patients should be advised to give up the use of tobacco in any form. It is much easier in the long run for the patient to stop smoking completely and suddenly, than to try to smoke less, or to attempt to reduce the amount gradually before stopping. I describe the blood supply to the heart in simple terms and point

out what is known about the effect of tobacco on the coronary circulation. This advice is based on the following observations.

1. There are a few patients who experience precordial distress on smoking, so-called "tobacco angina." Others have an awareness of the heart on smoking which they may describe as "palpitation."

2 In some persons smoking induces significant changes in the electrocardiogram. These changes are not unlike those induced by exercise and by the anoxemia test.

3. Smoking increases the heart rate and the blood pressure

4 Smoking decreases the temperature of the fingers and toes.

5 Smoking decreases the blood supply to the periphery of the body. Presumably this effect is the result of peripheral vasoconstriction. By inference the coronary vessels may participate in the vasoconstriction

6 Its deleterious effects in *Buerger's disease*, a disease of the peripheral arteries, are well known If adequate amounts of harmful substances are formed while smoking to affect the peripheral arteries in this disease, the inference may be made that they would be present in adequate amounts to affect other vessels in the body, such as the coronary arteries, especially if they are sclerotic

The observations of Levy and his associates on the effects of nicotine on the circulation did not show any striking difference between its effects in normal subjects and in patients with cardiac disease, except in susceptible individuals. The immediate effect on the circulation of smoking regular cigarettes was due to the nicotine in the tobacco Stewart and his associates showed that smoking decreased the peripheral blood flow in subjects in the older age group with vascular disease just as it did in younger, normal individuals, the changes, however, in peripheral blood flow (increase), blood pressure (rise), heart rate (increase), rectal temperature (rise), and average skin temperature—especially of hands and feet—(fall) were "less marked" in patients in the later decades than in normal young subjects Roth and Sheard have shown that at the height of the peripheral vasodilatation after oral ingestion of alcohol, smoking induced the same degree of vasoconstriction as in the control period before the ingestion of alcohol This observation refutes the common notion that the ingestion of alcohol will counterbalance the effects of smoking.

The patient is told frankly that in most instances we cannot prove that smoking is deleterious and that, in his own case, it may not be possible to detect any objective or subjective improvement if smoking is discontinued (It is also recalled that neither can any benefit from its use be demonstrated) In depriving the patient of tobacco the physician may appear to be generous by pointing out the somewhat liberal use of alcohol which is permitted

The physician should weigh the consequences of the continued use of tobacco against the optimal degree to which the course might be altered by discontinuing it In a very old person little might be gained by having the patient go through the discipline of giving up the habit Not all patients with coronary artery disease show changes in the electrocardiogram or in blood pressure with smoking. Many individuals have smoked since adolescence without showing any untoward effects

from its use. In spite of these arguments against the amount of benefit which might accrue from giving up smoking, I feel much more secure in the management of the angina patient when smoking is discontinued.

Drugs

The drugs which are most effective in the treatment of angina are vasodilators. They have *two objectives* and there are therefore two phases of therapy: increase in coronary blood flow and consequent relief of pain in the immediate attack, and prevention of attacks of pain or reduction in their frequency or severity by increasing the coronary reserve

Vasodilators

NITROGLYCERIN. Nitroglycerin is one of the most effective of the drugs available for the treatment of angina pectoris It gives relief from the symptoms so consistently and promptly that it is often employed in a diagnostic test for this syndrome

In the patient's first trial of the drug I recommend that only 0.0004 Gm. be given to test its effect on pain and to discover the magnitude of the side effects, such as sensations of pounding. The drug should be administered to the patient for the first time while the physician is present, so that the patient can be reassured about the side effects. *Patients should be forewarned about pounding of heart and throbbing of vessels*

Hypodermic or sublingual tablets should be ordered. The tablets should be fresh and should dissolve readily Advice is given about placing the tablet under the tongue. In a fresh preparation the effect should be expected within a few seconds. Patients should rest while the drug is taking effect If the small amount of the initial dose gives moderate but not complete relief and if the side effects are not too distressing, *the amount should be increased to 0 0006 Gm.* The drug may be repeated as often as required—if necessary as often as every hour. If the patient is unable to arrange his activities so that frequent attacks of angina can be avoided or kept within reasonable limits, other measures for the control of pain should be sought Nitroglycerin may be used as a preventive measure, that is, to meet a stress which usually precipitates an attack. For instance, if a patient must walk up a flight of stairs, nitroglycerin may be taken beforehand

Nitroglycerin is a vasodilator drug and the coronary circulation participates in the general vasodilatation With the coronary vasodilatation an increased amount of blood is supplied the cardiac muscle and pain is dissipated In those instances in which marked arteriosclerosis of the coronary vascular tree is inferred, it may be difficult to understand how *significant changes in caliber of the coronary vessels can be secured.*

AMYL NITRITE. The inhalation of amyl nitrite from a crushed ampul may be effective in relieving pain. Amyl nitrite is used because of its vasodilator effects. It acts quickly and its effect is fleeting It is used less frequently now than formerly In the long run nitroglycerin is more useful and its effects are of longer duration

ALCOHOL. Brandy or whisky may be used to give relief from an attack, or as a *preventive measure* in spite of Riseman's experience, which failed to show that attacks of pain were prevented or reduced in severity after the ingestion of

alcohol. For my part, I allow patients moderate amounts of alcohol daily as medication; I have not seen a single instance of alcoholism result from its use in this fashion The beneficial effect of alcohol may be in part attributed to its analgesic effect. It may also dilate the coronary vessels.

AMINOPHYLLIN. Aminophyllin 0.1 Gm to 0.2 Gm. may be given orally three or four times a day It may provide vasodilatation of longer duration than that from nitroglycerin Attacks of angina may be prevented or lessened in severity and frequency by its use. Both Levy and Stewart have reported reversal of the positive anoxemia test by this drug.

If a small amount of food such as a biscuit is eaten after the drug is taken, gastric distress and "heart burn" are not likely to occur

A recent paper has again reported the prevention of attacks of angina by aminophyllin given intravenously (Bakst) Aminophyllin can be given in larger amounts by rectum 0.5 Gm. two or three times a day as suppositories.

KHELLIN Anrep and his associates have recently described benefit in the treatment of anginal pain from the use of khellin, derived from the fruit of *Ammi visnaga*, a plant known in Arabic as "Khella," which grows wild in eastern Mediterranean countries It has been found to have a coronary vasodilator effect since it increases the coronary sinus outflow in heart-lung preparations It is apparently about four times more effective than aminophyllin in the relief of individual attacks and as a preventive They recommend that it be given orally in 50- to 100-mg. amounts three times a day or intramuscularly in 100- to 200-mg doses. It has few side effects and is not toxic even after prolonged administration It has no effect on the bleeding and coagulation times. These authors reported a high incidence of improvement following the use of this drug and were of the opinion that in certain patients the collateral circulation may have been improved. Improvement was apparent after three to four days of use of the drug in mild and moderate cases and after seven to ten days when the symptoms were more severe Optimal improvement occurred after two weeks' treatment The drug is cumulative and is excreted from the body slowly Hultgren *et al.*, using objective tests, report that patients with angina were not benefited by the use of this drug

ERYTHROL TETRANITRATE Erythrol tetranitrate in 0.03- to 0.06-Gm amounts three times a day may be used to prevent or lessen attacks of angina It may prevent nocturnal attacks of pain when it is given at bedtime

THEOBROMINE SODIUM ACETATE Theobromine sodium acetate (enteric coated) in 0.5-Gm amounts three time a day may be used. It is one of the most effective drugs of this group of vasodilators It is also a mild diuretic.

Other Drugs

PHENOBARBITAL. If the patient is high-strung, under tension, and apprehensive, phenobarbital 16 to 32 mg three times a day may be useful as a sedative.

MORPHINE Morphine should not be used in the treatment of angina pectoris The disease may go on for many years and the continued use of this drug may lead to addiction This restriction does not apply to the use of morphine in myocardial infarction, or to its use in the terminal stage of the disease, or when the patient has continuous pain.

QUINIDINE. Quinidine 0.2 to 0.3 Gm. three or four times a day has been recommended in the treatment of angina pectoris. I do not like to use quinidine for this purpose, because it is a myocardial depressant. From the nature of angina pectoris prolonged use would be required.

COBRA VENOM AND TISSUE EXTRACTS I have had no experience with cobra venom or tissue extracts in the treatment of angina pectoris. I do not think that the reported data indicate any special usefulness.

ATROPINE. I do not recommend the use of atropine in the treatment of angina because it increases the heart rate and induces uncomfortable side effects, such as dryness of the mouth, dilatation of the pupils, and even disorientation in older patients.

TESTOSTERONE. Testosterone propionate has been claimed by some investigators to decrease the severity of angina or to free patients of attacks completely. On the other hand other observers ascribe no benefit to its use. The balance of evidence seems to indicate that it is without specific effect on angina, although patients may have a sense of well being from using this drug which may make the discomfort more acceptable. Its effect on nitrogen metabolism may cause weight gain. It is given by frequent intramuscular injections, by the oral route daily, or by subcutaneous implantation of pellets at intervals of several months.

POTASSIUM IODIDE. I have not personally observed any benefit from the use of potassium iodide in the treatment of angina pectoris. It is said, however, to be of benefit not only in the angina of syphilitic heart disease, but also in angina due to coronary artery disease

DIGITALIS. Digitalis has no place in the treatment of the pain of angina pectoris [illegible] present. [illegible] The [illegible] heart disease who are not in failure. Digitalis given to anginal patients may cause precordial pain, presumably because of the decreased amount of blood available for the coronary circulation, when the cardiac output is decreased.

INJECTION OF TRIGGER AREA. The relief of cardiac pain by local block induced by infiltration of trigger areas with procaine hydrochloride (0.25 to 0.5 per cent in physiologic saline) or by spraying the skin with ethyl chloride has no place in the treatment of pain recognized as angina pectoris or of pain associated with myocardial infarction. In the cases I have seen treated by others a large psychic element seemed to account for any benefit Moreover the occurrence of serious complications from infiltration of muscles in the neighborhood of vital tissues makes this procedure inadvisable

HEPARIN. The finding of Gofman that the intermittent administration of heparin intravenously in 50- to 100-mg amounts to patients with severe angina results in relief from this symptom for several days afterward awaits confirmation.

Carotid Sinus Pressure

From our experience in the application of pressure to hypersensitive carotid sinuses, I do not think that it is wise to employ carotid sinus pressure as a measure to stop anginal attacks.

X-RAY TO ADRENAL REGIONS

There is no good evidence that x-ray radiation of the adrenal regions favorably influences the symptoms of angina pectoris.

MEDICAL THYROIDECTOMY

6n Propylthiouracil

Attempts have been made by reduction of the basal metabolic rate to diminish the demands made upon the heart and by this means to decrease the occurrence and severity of angina pectoris. For this purpose 6n propylthiouracil may be used. Although total surgical ablation of the normal thyroid gland, when this procedure had a short vogue a few years ago, was believed to be required to affect the incidence of angina, it has been found that the level of the basal metabolic rate can be lowered sufficiently to provide benefit with propylthiouracil without the induction of myxedema The reduction of the basal metabolic rate 15 to 20 per cent reduces the work of the heart sufficiently.

The effects of propylthiouracil should be closely observed. The basal metabolic rate should be recorded frequently, the count of the white blood cells together with the differential count and estimation of the blood cholesterol should be made at regular intervals Of greater importance, however, is that any change in the patient's state of well being should be reason to discontinue the drug and to repeat all of these tests at once The size of the thyroid gland should be observed and signs and symptoms of frank hypothyroidism should be avoided. Toxic manifestations from this preparation are uncommon enough for the physician to have more of a sense of security than was possible with thiouracil.

Propylthiouracil blocks the formation of thyroid hormone. It takes several months for the gland to empty itself of the hormone which it already contains For this reason patients may be taking the drug four to six months before any reduction in basal metabolic rate occurs and before alteration of symptoms can be expected. In some euthyroid patients lowering of the basal metabolic rate cannot be secured by this drug This drug deserves a trial in those patients with angina who do not secure adequate relief from the usual medical management and who are not suitable for upper thoracic sympathetic ganglionectomy, or for those whose symptoms may not be severe enough to warrant the surgical procedure. The dosages of this drug are given on page 329.

Radioactive Iodine

Radioactive iodine has been used to induce myxedema in patients with angina, with the intent of reducing the work of the heart. Blumgart and associates have reported some measure of success. The procedure is, however, in the exploratory stage Certain patients suffering from both angina and congestive heart failure experienced alleviation of both manifestations. In the use of this measure patients become permanently myxedematous; when this state is attained they are given enough thyroid extract to achieve the maximum relief from their cardiac symptoms with the minimum of discomfort from myxedema. The optimal basal metabolic

rate for most patients is in the range from -15 to -25 per cent. For this reason patients with initial basal rates below -15 per cent should not be treated.

Patients may have a transient period of thyroiditis seven to ten days after exhibition of the drug; a few weeks later there may be exacerbation of the symptoms of angina due to transient increase in basal metabolic rate with release of thyroid hormone from the gland. This may be of such magnitude that patients with severe angina may not tolerate it. This stage may sometimes be prevented by the previous use of 6n propylthiouracil Four months or longer are required for the full benefit from the use of I^{131} to be realized.

Radioactive iodine should only be given to patients with intractable angina and at the present time should not be used under the following circumstances: (1) if the patient can be kept comfortable and moderately active by the use of nitroglycerin and by management of activities; (2) if the patient is suitable for a trial period on propylthiouracil; and finally (3) if it is felt that the patient can be safely carried through upper thoracic sympathetic ganglionectomy. The subsequent history of those patients who have undergone this treatment will be followed with the greatest interest. Whether the progression of arteriosclerosis will be accelerated is a pertinent issue.

Surgical Measures

Most patients suffering from angina carry on very well on a medical regimen, but there are some in whom the pain is so severe or so frequent, or whose activities require such rigid restriction for comfort, that other approaches have to be considered. A wide variety of surgical procedures have been suggested and have been given trial. The physician should be able to evaluate the relative merits of the different procedures and their appropriateness for the individual patients

Total Thyroidectomy

Total thyroidectomy had a short vogue, but is now rarely used. Its objective is reduction of the basal metabolic rate so that the demands on the heart are diminished. Total ablation of the gland is necessary if any benefit is to be recognized. This results in the artificial induction of a profound myxedematous state with all the disagreeable effects which this disease implies. I have not subjected any patients to this form of therapy. I have, however, had occasion to see patients who were subjected to this procedure at other clinics and this experience, though small, has led me to the conclusion that the artificial induction of a disease (myxedema), with such profound consequence in itself, is rarely to be undertaken in the treatment of angina It is an interesting concept and would have found more usefulness if its ends could have been attained short of such a drastic, irreversible procedure The objectives of this procedure can now be attained in some patients by the use of propylthiouracil

Interruption of Pain Pathways

One of the most effective measures for the treatment of severe angina for which something more than medical treatment is required, is the interruption of the pain pathways. Visceral afferent fibers from the heart pass through the ganglionated

chain and enter the cord by way of the posterior nerve roots. They have their cells of origin in the posterior ganglion just as the somatic afferent fibers do and enter the cord, synapse in the posterior horn with second neurons which cross, and ascend in the spinothalamic tract. All pain impulses coming from the heart, regardless of what nerve they travel, enter the cord between the first and fifth thoracic segments The innervation is bilateral.

The lack of pain signals does not appear to be dangerous. Moreover on severe exertion patients who have undergone surgical treatment experience substitute symptoms among these are choking sensations, discomfort in the neck, pain in the teeth and in the lower jaw. These can be used as guides to modify activity. The pathway for the pain in the teeth and at the angle of the jaw is not known.

Three procedures are available for the interruption of the pain pathways.

INJECTION OF POSTERIOR ROOT GANGLIA T_1 TO T_5 INCLUSIVE WITH 95 PER CENT ALCOHOL. This procedure results in necrosis of the nerve tissue. The upper four or five thoracic ganglia may be injected, T_1 to T_5 inclusive. After alcohol injection the following complications have been encountered: (1) Pleural effusion may occur early after the injection, (2) Later, intercostal neuralgia due to radiculitis may make the symptoms caused by this complication outweigh the benefit of relief from angina, (3) If the needle should enter the subarachnoid space complete transverse myelitis may result and may give permanent damage, and (4) Horner's syndrome—small pupil, drooping of the lid, and loss of sweating of the face—may occur

Relief from pain may last for months or years If pain is bilateral, one side should be injected at a time. The procedure is carried out under local anesthesia, and the patient may be in the sitting position. The procedure has the advantage that it can be used in patients who are too sick for surgical procedures which may require a general anesthesia On the other hand the mental strain of the procedure and the discomfort while it is being done under local anesthesia may precipitate coronary thrombosis.

POSTERIOR ROOT SECTION (RHIZOTOMY) OF T_1 TO T_5 INCLUSIVE. The second method of interruption of pain sensation is by posterior root section of T_1 to T_5 inclusive, on one side or bilaterally if pain has such distribution. Both sides can be operated upon at one exposure through a laminectomy. Intratracheal ether-oxygen anesthesia is used. In the experience of White and of Ray, this operation has a place in the treatment of a few patients It has been effective in the patients *I have observed Recovery is rapid, patients may be ambulatory in ten days to two* weeks. There will be sensory loss in the upper thoracic dermatomes. Since the region is anesthetic, patients should be warned especially about the danger of burns

The occasions for the use of this operation are more restricted than the operation of upper thoracic sympathetic ganglionectomy, which is the procedure of choice Patients who have pain very frequently and of great severity should be considered, especially if the pain is bilateral, since both sides can be done at one operation Patients with congestive heart failure should not be subjected to this procedure because they have to lie prone on the abdomen during operation and cannot be propped up, and considerable time is required for the laminectomy Patients should not have suffered recent coronary occlusion, nor should they have

evidence of too marked cardiac damage. The interruption of the pain fibers is permanent. *There are no ocular and sudomotor changes of the face and neck and* upper extremity, effects that accompany alcohol injection and sympathectomy. The painful neuritis of alcohol injection is avoided. There is noninterference with the sympathetic mechanism controlling the heart. The procedure affords the opportunity of treating bilateral pain with one operation. It can be employed when previous alcohol injections have not been successful. It is, however, an extensive operation and for this reason upper thoracic sympathetic ganglionectomy (description following) can be more readily carried out.

Upper Thoracic Sympathetic Ganglionectomy. White recommends upper thoracic sympathetic ganglionectomy as the surgical operation of choice in the treatment of angina pectoris. The operation is carried out through a posterior approach with resection of the central end of the second rib and its transverse process. Ether-oxygen anesthesia is given through an intratracheal catheter with the patient in the lateral position. The posterior approach allows good exposure for resection of the inferior cervical ganglion through the third thoracic ganglion White states that when the inferior cervical and the first thoracic components of the stellate ganglion are separate as a dumb-bell shaped structure, removal of the lower portion is sufficient, but when fusion has taken place the entire ganglion should be resected. It is not necessary to carry the resection upward into the cervical region but it is essential to follow the chain downward to include at least the third thoracic ganglion.

In experienced hands the operation can be done within an hour with a minimal risk of operative and postoperative complications. Sympathectomy at this level induces a Horner's syndrome with ptosis and myosis. If the pain is limited to the left side, *only this side is operated upon. (After operation the left side will be* warm and dry and the right, unoperated, is cool and moist) On the other hand if the pain is bilateral or if pain appears later on the unoperated side a second ganglionectomy may be performed on the opposite side White has had no deaths since the routine use of intratracheal anesthesia and the recent advances in chemotherapy for treating postoperative pneumonia

Lindgren and Olivecrona carry the resection of the chain as low as the fourth or even the fifth ganglion in order to prevent occasional pain low in the precordial region. In White's recent experience with this procedure he has found the results so satisfactory that he thinks upper thoracic sympathetic ganglionectomy the preferable surgical procedure in all but the worst operative risks. He recommends that the operation be done in two stages when the pain is bilateral. Ray from an experience with both operations is of the opinion that this operation has a wider application than posterior rhizotomy.

These three procedures—paravertebral alcohol injection, upper thoracic sympathetic ganglionectomy, and posterior rhizotomy—find their widest application in angina of the most common type, that due to coronary artery disease resulting from arteriosclerosis The procedures are also available for patients with syphilitic aortitis and aortic insufficiency and rheumatic heart disease (aortic stenosis, aortic insufficiency) who have pain. Either upper thoracic sympathetic ganglionectomy or posterior rhizotomy are available for patients who can withstand the operations,

alcohol injections for those too sick to be subjected to the former two. As further experience has been gained, upper thoracic sympathetic ganglionectomy has come to have a wider application than posterior rhizotomy.

SYMPATHECTOMY FOR ANGINA PECTORIS AND PAROXYSMAL TACHYCARDIA. When patients suffer from angina pectoris and attacks of auricular paroxysmal tachycardia or fibrillation associated with pain during the paroxysms and when the paroxysms of tachycardia are resistant to quinidine and other medical measures, sympathectomy has been found to give relief from the pain, and in all likelihood may lessen or abolish the paroxysms of tachycardia Jonnesco described such a combination of symptoms. White's patient, exhibiting this group of symptoms and signs, secured relief for six months following paravertebral alcohol injections; a second paravertebral alcohol injection was, however, less effective, since it lasted only one month. This patient was a good surgical risk and in retrospect the opinion was expressed that bilateral resection of the upper thoracic sympathetic chains should have been done

STELLATE GANGLIONECTOMY. Coffey and Brown advocated stellate ganglionectomy in the treatment of angina, but if pain is mediated only in part or totally through other fibers this procedure is ineffective. This procedure is no longer used

Other Surgical Measures

PERICORONARY NEURONECTOMY AND LEFT CORONARY SINUS LIGATION Fauteux has resected the cardiac nerves adjacent to the coronary arteries together with ligation of the coronary vein in a few patients for the relief of angina pectoris. It is doubtful how much collateral circulation can be provided after ligation of the coronary vein. The procedure requires wide exposure of the heart and is an operation of the order of magnitude of the Beck procedure described below.

SURGICAL PROCEDURES TO INCREASE THE BLOOD SUPPLY TO THE MYOCARDIUM. In attempts to relieve angina several operations have been devised which have as their objective an increase of the blood supply to the heart muscle or the provision of a new supply of blood from remote sources to augment the diminished flow to the cardiac muscle through the coronary vessels:

1. O'Shaughnessy brought vascular-rich omentum through an opening in the diaphragm and sutured it to the heart muscle.

2 Beck has attached a pedicle of pectoral muscle to the heart muscle and reported benefit presumably due to a new blood supply accompanying the transplanted skeletal muscle This operation has been attempted only in patients who have a very restricted coronary circulation, besides it is an operation which cannot be done quickly For these two reasons the operation has a high mortality rate.

3 Beck has also attempted to encourage a new vascular supply to the heart muscle by the induction of pericardial adhesions following the introduction of bone dust and other irritating agents into the pericardial cavity The adhesions would presumably carry a blood supply with them.

4 Thompson has attempted the same objective by the use of powder blown into the pericardial cavity This latter procedure may give rise to grave interference with the dynamics of the heart resulting in chronic constrictive pericarditis, an occurrence which has been observed clinically.

5. Attempts have been made by Carter, Gall, and Wadsworth to increase the blood supply to the heart muscle by approximating lung to the visceral pericardium.

6. Beck and his associates have recently reported on the revascularization of the heart by graft of a systemic artery to the coronary sinus. Based on observations carried out in dogs, a graft of brachial artery was used to connect the aorta to the coronary sinus in one patient. They had been reassured by the animal experiments that the coronary sinus could sustain arterial pressure. The results of this operation have not been published beyond the statement that the patient tolerated the surgical procedure.

7. More recently Beck and his associates have reported upon another procedure which is carried out in two stages In the first stage a free vein graft (basilic, cephalic, or jugular) is placed between the coronary sinus and the aorta, initiating an arteriovenous fistula In the second stage, carried out three weeks later, the coronary sinus at the ostium of the sinus in the right auricle is partially ligated. The vein tolerates the increase in pressure; its wall increases in thickness. Twenty-three of 28 patients survived the first stage and 13 of these had the second stage. The results in these appeared to be favorable, but sufficient time has not elapsed for an adequate appraisal.

The beneficial effects of these procedures have not been convincing enough to be applied by other surgeons than those making the original observations From observations of patients with chronic constrictive pericarditis I am convinced that very little blood can be carried to the heart muscle by adhesions, and certainly not enough to warrant the risk involved in the formation of adhesions. The observations in normal dogs with a normal blood supply need not apply precisely to patients with angina pectoris in whom the coronary circulation is diminished due to narrowing of coronary vessels or to their occlusion.

ANGINA DECUBITUS

Occasionally patients have anginal attacks with such frequency, even at complete bed rest, that angina decubitus is said to be present. Patients may experience panic with each episode, sweating is profuse. The use of oxygen may give some relief. Nitroglycerin may be given as frequently as required and whenever its effects wear off In some instances morphine may be required to provide relief from pain and an opportunity for sleep.

If the patient is not too poor a risk paravertebral alcohol injection may be attempted. The prognosis is grave.

SUMMARY

By a wise selection of the measures which have been described, many patients with angina continue to lead useful, active lives for many years. Some go on to suffer heart failure, others to suffer myocardial infarction, a few succumb to sudden death, and others die from intercurrent disease.

From the foregoing text it is apparent which of these measures are most useful. In brief, the most effective are: regulation of the patient's activities, orientation

about pain, moderate sedation with phenobarbital, the use of nitroglycerin for acute pain and of one of the slower acting vasodilators as a preventive measure, and the moderate use of alcohol. For a few patients reduction of the basal metabolic rate by the use of an antithyroid drug may be beneficial

For more severe, more frequent pain in a few patients, upper thoracic sympathectomy, posterior root section, alcohol injection—in short, one of the surgical measures for interrupting pain sensation—should be considered These surgical measures should, perhaps, be offered to patients more frequently. Many patients have been able to resume activity after operation. The marked change in mental attitude, along with the relief from pain as well as the relief from the fear of pain, the recovery from loss of sleep and the possibility of drug addiction should be given adequate weight in deciding about operation. Other operative procedures [illegible]

established

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CHAPTER 13

Myocardial Infarction, Coronary Thrombosis, Coronary Occlusion

PATHOLOGY

Myocardial Infarction Due to Coronary Occlusion Resulting from Coronary Thrombosis

Myocardial infarction results from interruption of the blood supply to the heart muscle. The most common cause is occlusion of an arteriosclerotic coronary artery by acute coronary thrombosis An atheromatous lesion of the intima is the site of thrombus formation. The portion of vessel occluded may show localized arteriosclerosis, but most commonly there is generalized arteriosclerosis of all of the coronary arteries to varying degrees (Fig 37). With *occlusion of a coronary artery* [illegible] l is interrupted. [illegible] area with blood [illegible] without delay. If this does not occur necrosis of tissue proceeds without repair and the infarcted area of the myocardium is weakened This may cause the appearance of signs and symptoms of heart failure. Rupture or an aneurysm of the ventricle may develop with different degrees of thinning and weakening of the ventricular wall

Gofman is of the opinion (1) that the occurrence of myocardial infarction is positively related to elevation of S_f 12–20 lipoprotein levels; (2) that the recurrence rate of myocardial infarction in patients with coronary artery disease is positively and highly related to the S_f 12–20 lipoprotein levels; and (3) that the depression of high S_f 12–20 levels by dietary restriction of fat and cholesterol has brought about significant decrease in the recurrence of myocardial infarction in patients with coronary artery disease On the other hand Keys thinks that the concentration of the G substances (S_f 10–20) is not any more closely related to arteriosclerosis than is the total serum cholesterol.

Coronary Occlusion Without Myocardial Infarction

If narrowing of coronary arteries takes place slowly a good compensatory collateral circulation may develop between the branches of the coronary system. Now complete closure of one of these vessels from thrombosis may occur without signs and symptoms and without evidence of myocardial infarction at autopsy.

Myocardial Infarction Without Coronary Occlusion

In other instances an area of heart muscle may show infarction without closure of the vessels supplying the area. The infarction may occur in shock or in any state associated with prolonged fall in blood pressure. This is especially the case if the blood pressure has been high and then falls to a low level. If the fall in blood pressure takes place in the presence of coronary vessels which are already arteriosclerotic, the amount of blood supplying the heart muscle may be inadequate and myocardial damage more readily occur.

Patients who are thought to have myocardial infarction without coronary occlusion should be treated as though coronary occlusion had occurred. The aftertreatment, prognosis, and implications are, however, different. Myocardial infarction without closure of vessel may occur during operations, especially when an anesthetic is used which is associated with fall in blood pressure. It may occur in patients with hypertension and coronary artery disease who are subjected to splanchnic resection, especially if a marked fall in blood pressure results When narrowing of a coronary artery progresses until closure finally takes place, there may be little or no pain, but the other manifestations of myocardial infarction may be recorded

Coronary Occlusion Due to Coronary Embolism

Closure of a coronary artery with myocardial infarction may result from a coronary embolism This may occur in subacute bacterial endocarditis.

Terminology

At one end of a scale is ischemia resulting in angina pectoris and at the other is the ischemia which is prolonged and persistent and results in necrosis of heart muscle—in short, gives rise to myocardial infarction, the most common cause of which is coronary occlusion due to coronary thrombosis. *Myocardial infarction* is the best term to use for this series of events—with the qualification that it is due to coronary occlusion caused by coronary thrombosis when this is the projected mechanism For those instances in which myocardial infarction occurs without thrombosis, as in shock, it may be stated that it is myocardial infarction *without* coronary occlusion The diagnoses most commonly applied clinically, however, are myocardial infarction, acute myocardial infarction, coronary thrombosis, and acute coronary thrombosis

There is a variety of coronary insufficiency, the description of which has caused confusion. I refer to those instances in which the ischemia is of intermediate severity—between that resulting in angina pectoris and that giving rise to myocardial infarction The pain is of longer duration than in angina, comes on at rest or on

exertion, is not relieved by rest or nitroglycerin, and may be associated with sweating, pallor, transient fall in blood pressure, and electrocardiographic changes which are more persistent than in angina. Evidence of necrosis of muscle does not follow (fever, leukocytosis, rise in sedimentation rate). Recovery may be prompt. Such episodes may follow shock, anoxemia during anesthesia, and emotion, to mention a few of the most common forerunners. The names "coronary failure" and "coronary insufficiency" have been suggested for such episodes.

Other terms which have been suggested to designate angina pectoris and myocardial infarction are "acute coronary insufficiency without acute occlusion" and "acute coronary insufficiency with acute occlusion," respectively. Since there is coronary failure with angina pectoris this term does not appear to be appropriate, and since "coronary insufficiency" has long been used with a broader meaning it does not appear wise to restrict its meaning. It might be better to use a longer expression such as "severe anginal attack with persistent ischemia not resulting in infarction" or "severe anginal attack with questionable infarction of the myocardium"—labels which are clear in their meaning even though it may not be possible to be dogmatic about all the episodes which come under observation.

Location of Infarction

The most common location of myocardial infarctions is in the anterior apical region of the heart, due to closure of the anterior descending branch of the left coronary artery The next most common location is the posterior base region, due to closure of the circumflex branch of the left coronary artery or closure of the right coronary artery. Septal involvement may occur. Myocardial infarctions in the two main locations usually give rise to typical electrocardiographic alterations and each type goes through a series of characteristic changes. Lateral, endocardial, and epicardial localizations can sometimes be postulated The extent of the electrocardiographic changes usually parallels the size of the infarct.

Multiple precordial leads aid in the diagnosis and localization of myocardial infarction. Unipolar derivations in certain instances may show abnormalities which may not be present in the usual CF derivations

Patients with myocardial infarction should be treated according to the whole clinical picture rather than by the electrocardiographic pattern exclusively. However, serial electrocardiograms have a valuable place in the observation and management of patients.

Electrocardiographic patterns may not be so easily identified in the presence of auricular fibrillation and of bundle branch block as when normal rhythm and normal QRS conduction respectively prevail

In the long run the anterior apex lesions are more severe than the posterior base ones. The lateral wall infarctions are not so sharply defined in electrocardiographic records, transient auricular fibrillation is said to be common in these.

Occasions arise when very extensive recent myocardial infarctions may cause death and yet the electrocardiograms may have shown only low amplitude of the QRS complexes and atypical changes in T waves and RS-T segments. Typical anterior apex or posterior base patterns or combinations of these two cannot be

detected. The damage has apparently been so extensive that the summation of all the effects causes aberrations which can be characterized merely as "atypical"

When the myocardial infarction extends through to the ventricular cavity and involves the endocardium, mural thrombi may form These may later be covered over by endothelium, or pieces of thrombus may break off and become the source of emboli This latter possibility forms one of the arguments for the use of anticoagulant therapy in myocardial infarction Mural thrombi may form later over an old scar after healing has occurred

Pericarditis

If the myocardial infarction extends to the outer surface of the heart, the *pericardium is involved and a sterile dry or fibrinous pericarditis results.* In anterior apex lesions a pericardial friction rub may be heard Pericarditis occurs also in posterior base lesions, but the friction rub of normal degree is more difficult or even impossible to hear unless the inflammation extends around anteriorly. The pattern of acute pericarditis in the electrocardiograms may complicate that due to myocardial infarction.

MYOCARDIAL INFARCTION DUE TO ACUTE CORONARY THROMBOSIS

Clinical Manifestations

The typical history of myocardial infarction due to acute coronary thrombosis is somewhat as follows The patient has precordial distress which persists. It may be unrelated to exertion, may have come on after a hearty meal, or may awaken the patient out of a sound sleep. The pain is described as "pressure," "vise-like," "constricting" It may radiate to the left arm, to the elbow or hand, to the throat, neck or occiput, to the back or to the left shoulder, or to the right side of the precordium and the right shoulder and right arm The patient has profuse perspiration There may be nausea and vomiting Nitroglycerin does not usually give relief Repeated doses of morphine may be necessary to provide relief. When the patient is seen at this stage his blood pressure may be slightly elevated owing to pain, he has an ashen gray pallor and may be sweating profusely Shortly the blood pressure begins to fall. Within a few hours the temperature rises, as does the white blood cell count. The heart sounds may be faint and cardiac irregularities may be recorded At this stage the electrocardiogram may not show any marked changes except slight elevation or depression of the RS-T segments. The ballistocardiogram may be grossly abnormal

Within 24 hours the temperature may be 39° to 39.5° C. and the white blood cell count around 18,000 The sedimentation rate may have begun to rise. Anterior apex or posterior base patterns may be apparent at this time A pericardial friction rub may be heard The fever usually runs its course in a week unless the damage is marked, and the sedimentation rate and white blood cell count reach their height in a week to ten days and then show a gradual decline and reach normal within a month The pain usually subsides within 24 hours and in uncomplicated cases is not expected to recur. After the appearance of the electrocardiographic pattern the

electrocardiogram usually goes through typical changes which take place over a period of several weeks to months before stabilization occurs or reversion to the preinfarction pattern is recorded. With rest in bed and control of symptoms convalescence may be without incident. In other instances the damage may be more severe and fever, leukocytosis, and rise in sedimentation rate may reach higher levels and be more prolonged. Extension of the thrombosis may occur, or an anterior apex lesion may be superimposed on a posterior base one or vice versa.

Patients may suffer several infarctions in succession. Thromboembolic phenomena may occur should mural thrombi be formed. The whole constellation of cardiac irregularities may occur: premature contractions, paroxysmal tachycardias, auricular fibrillation, and auricular flutter. Conduction defects up to complete heart block and bundle branch block occur if the septum is involved; they are more likely to be seen in posterior base involvement of the heart.

The symptoms of myocardial infarction may be very mild and last only about an hour or may persist for days in spite of morphine, oxygen, and other therapeutic agents

In *syphilitic* involvement of the aorta and aortic valve, deformity of the coronary ostia may give rise to angina with decrease in coronary blood supply or, if the opening is progressively narrowed to occlusion, with thrombosis. When closure occurs signs and symptoms of myocardial infarction may be added to those already present If the closure has resulted from too vigorous specific therapy this should be discontinued at once The patient is treated as is any other patient suffering from acute coronary occlusion One must recall that patients with aortic insufficiency due to syphilis may suffer from angina

Treatment

General Principles

The treatment of myocardial infarction is essentially the same whatever the events causing the damage. Adjustments may be made in the schedule depending upon the setting in which the cardiac damage occurred. If myocardial infarction occurs in the course of some other disease, the latter disease may require active therapy and adjustments are made by balancing the requirements of the two conditions; the more pressing of the two may take momentary precedence An example would be coronary thrombosis occurring after a surgical procedure In other instances the primary disease may be temporarily relegated to the background. For instance, the specific treatment of syphilitic heart disease is discontinued when closure of a coronary ostium occurs and results in myocardial infarction. When acute coronary thrombosis occurs in the course of a surgical operation which might ordinarily be followed by early ambulation, the patient now remains in bed as any other patient suffering from this accident.

RATIONALE. The rationale of the treatment of acute myocardial infarction is in the first place to give the patient's heart as much rest as possible in order to provide for healing of the damaged area, and in the second place not to demand more work of the heart than the minimum in order not to strain an organ which has suffered insult. Since the heart cannot be put at complete rest as can be done with some parts of the body while they are undergoing healing, the best that can

be done is to provide enough mental and bodily relaxation for the patient to keep him during the healing process at almost basal levels of activity. During the period of healing the damaged cardiac muscle is replaced by fibrous tissue which is non-functioning as contractile tissue. Collateral circulation must then be established rapidly so that a minimal amount of death of muscle tissue occurs. The heart which has a scar and has been at rest for some weeks should then be restored to activity gradually in order not to precipitate failure or angina, and in order not to exceed its functional capacity after final restoration of activity.

In the progressive changes in the heart muscle, necrosis is at a maximal degree around seven to ten days after coronary thrombosis occurs, and at this time the muscle wall is weakest. It is especially important that activity should be restricted at this time in order not to precipitate rupture of the ventricle. Healing is fairly well along at the end of three weeks but it is only after four, five, or six weeks that the replacement by scar tissue is advanced. Continuation of healing goes on for years, probably accompanied by improvement in collateral blood supply, if the gradual decline in negativity of T waves in favorable cases may be interpreted in this manner. It is well recognized, however, that electrocardiographic changes cannot be correlated with functional capacity.

Plan of Treatment

REST IN BED. The patient is put at complete rest in bed. This is best carried out in a hospital even when good home care is available and the attack is mild; it is only when the patient is extremely ill that removal to a hospital should not be undertaken. The rapid action of the medical house staff in emergencies may be life-saving. If the patient should refuse hospitalization, or if the physician thinks that treatment can be satisfactorily undertaken at home he ought to insist upon complete bed rest. The patient is lifted onto the bedpan, he does not go to the bathroom or have a commode at the bedside. Customary measures, such as turning the patient, having him take deep breaths, and having him move the legs frequently, to prevent stasis and expand the lungs, are carried out. The "chair" treatment—in which patients sit in a chair in the day time—is not recommended (see p. 315).

RELIEF OF PAIN. *Morphine* 16 mg. is given by hypodermic injection if pain is present. If pain is severe and the first injection gives no relief in thirty minutes, 16 mg. more may be given. If pain is very severe, larger initial doses of morphine may be required. Patients with severe pain may require and can tolerate a large amount over the first 24 hours without the appearance of toxicity. The drug may be required every four hours. For intractable pain 2.5 to 15.0 mg. morphine may be given slowly intravenously—dissolved in 5 to 10 cc. of sterile water or saline—with close attention to the respiratory rate.

If patients cannot take morphine because of sensitivity, *pantopon* 1 cc. (20 mg.) or *demerol* 100 to 150 mg. may be used as substitutes. When pain is less severe, *codeine* may be sufficient, 32 mg. being given orally or by hypodermic. I rarely use *aspirin* to relieve pain in coronary thrombosis, not only because the patients are sick and require a more effective drug, but also because it may cause additional sweating, with fall in temperature; this invalidates the temperature pattern as a guide in the patient's progress. At this stage I try not to use *phenobarbital* because

it may lower the blood pressure and be misleading if the physician is using the course of the blood pressure as a guide to progress or in equivocal cases as a diagnostic sign. When it must be used phenobarbital is given in 16- to 32-mg. amounts.

TREATMENT OF PERSISTENT PAIN. If pain persists after the first 24 to 48 hours, oxygen is continued and aminophyllin 0.1 Gm. four times a day must be used. *Whisky 30 cc. three or four times a day* may give relief. See Chapter 12 for the rationale of these drugs.

Penicillin may forestall possible pulmonary infection because of pulmonary stasis from the patient lying quietly and from the restriction of breathing by the use of sedatives.

SLEEP. Morphine may be the best drug to provide sleep for a few nights. However, when pain requiring morphine has subsided, one of the quick-acting drugs such as *sodium pentobarbital* 0.1 Gm. may be used. This may be repeated after a three- to four-hour interval. Its effect may be enhanced by 30 cc. of whisky at bedtime. If heart failure occurs with dyspnea, morphine may be required beyond the first few days.

FLUID INTAKE. Up to 1500 to 1800 cc. a day may be allowed if there is no evidence of congestive heart failure.

DIET. A liquid diet is provided for the first few hours or perhaps for 24 hours if the patient is severely sick. A soft diet may be allowed for milder cases. The diet is limited to easily digested, mostly carbohydrate foods during this early period. Milk toast, soft eggs, custards, cereals, or ice cream may be adequate. Tea and coffee may be allowed as desired if there is no sensitivity to them. After a few days a more liberal diet is provided when it can be taken: creamed chicken, chopped beef, baked potatoes, and easily digested puréed vegetables. Later the diet is liberalized with cream or clear soups, roast beef, broiled lamb chops, and steaks. Fried food, pork, leafy vegetables, and salads are not allowed and it is *best to forego* highly seasoned foods and sea foods. Desserts should be simple and easily digested: fresh fruits, stewed fruits, custards, gelatin, and ice cream. Vitamin supplements, especially of the B components, are provided in the early stages and may be continued. *Small portions of food are served so that overloading the stomach* does not occur. Whisky in 30-cc. amounts diluted with a little water may be taken a short while before meals.

As the patient progresses into convalescence still more liberal diets are allowed, with more selection permitted. Fried and gas-forming foods are withheld. Overeating should be avoided, so that in most patients gain in weight does not occur. When salt restriction is required it can be provided in any of the diet levels which are indicated and which have been mentioned. Diabetic patients should have the appropriate attention to diet requirements and to the use of insulin. Especial care is exercised that hypoglycemic shock does not occur with fall in blood sugar.

OXYGEN. If the patient has severe precordial pain, or if there is cyanosis or evidence of failure, oxygen is used promptly. An oxygen tent is the most satisfactory method but a mask will suffice if it alone is available. Oxygen may relieve the pain and is indicated *if heart failure is present. It is more expedient to use* oxygen

early than to wait for the status of the patient to become alarming Breathing 100 per cent oxygen for short periods may provide temporary relief from pain.

TREATMENT OF DEHYDRATION FROM VOMITING. Nausea and vomiting are usually not persistent enough to cause dehydration. Morphine may be a causative factor in persistence of nausea and vomiting in patients hypersensitive to this drug. Occasionally, however, nausea and vomiting are so severe and persistent that all oral feeding and medication must be discontinued. In this case adequate amounts of normal saline and 5 per cent glucose can be given by hypodermoclysis. Hyaluronidase may be added to hasten absorption and if there is much loss of fluid it may also be necessary to add potassium. Soluble vitamin B and thiamine may also be added to the hypodermoclysis fluid. It is safer to give fluid by hypodermoclysis than intravenously, as the latter method may increase the venous pressure and cause acute cardiac failure, although on occasion the slow absorption by this route makes intravenous administration necessary.

The volume of urine and its specific gravity should be observed. Care should be exercised to avoid a salt depletion syndrome from the loss of electrolytes in the vomitus. Serum electrolytes should be estimated daily, as should the carbon dioxide combining power of the blood and the blood urea nitrogen. As nausea and vomiting lessen, hot weak tea with a little sugar may be given first, followed by broth and later still by gelatin, custard, melba toast, and soft egg.

When all medications by mouth are discontinued, digitalis if required is given intravenously and *depo-heparin* may be used instead of dicumarol as the anticoagulant.

CATHARTICS. Early attention to the bowels is important. If morphine has been used constipation will occur. It is best to use an enema daily during this period to prevent marked constipation, distention, and fecal impaction It is also important to avoid straining at stool Within a few days the judicious daily use of a laxative will insure a soft stool without straining Mineral oil 30 cc. may be sufficient or it may be combined with milk of magnesia 15 to 30 cc For certain patients the addition of compound licorice powder 8 cc. or cascara sagrada 8 cc to the above mixture may be necessary A small dose of the combination of these three drugs provides an effective bowel movement daily without straining When distention occurs in the early course of myocardial infarction, turpentine stupes with a rectal tube give relief While turpentine is being used, should an oxygen tent be in operation, the patient must be removed from the tent and the oxygen flow interrupted

In some patients *abdominal distention* may be extreme This may involve the stomach and whole gastrointestinal tract There may be paralytic ileus This gives rise to discomfort, raises the diaphragm, and embarrasses the respirations. If nausea and vomiting are not present sodium phosphate may be given to initiate gastrointestinal motility. A rectal tube may be used, and hot compresses applied to the abdomen If distention increases it may be necessary to discontinue all oral feeding and institute suction with a Miller-Abbott or Wangensteen tube The fluid removed should be restored by hypodermoclysis, together with enough to provide for the fluid requirements, including electrolyte replacement. As distention decreases the tube may be clamped and trial periods of oral feeding of fluids attempted again; one

to one and one-half hours are allowed for the stomach to absorb the fluids and to empty, followed by another period of gastric suction. An oil retention enema or a magnesium sulfate (60 per cent solution, 30 cc.), glycerin (60 cc.), and water (90 cc.) enema may be useful. In all this care must be exercised that the therapeutic program allows adequate rest periods for the patient.

Anticoagulants

The use of heparin and dicumarol in the treatment of acute coronary thrombosis to prevent extension of the thrombosis, additional coronary thrombosis, mural thrombi, emboli, and venous thrombosis has been discussed in Chapter 4. The use of dicumarol to prevent coronary thrombosis is also discussed in that chapter.

Drugs Contraindicated

Patients have a better prognosis when only those drugs are used for which there are definite indications. There are a few drugs which I do not recommend for use in the acute stage of coronary thrombosis.

NITROGLYCERIN. It appears best not to use nitroglycerin in the routine treatment of precordial pain due to acute coronary thrombosis. If the coronary artery is thrombosed, it is obvious that nitroglycerin cannot induce vasodilatation. I rely upon the use of morphine and oxygen for the relief of pain. After the pain associated with the occurrence of thrombosis some patients continue to have transient angina on the slightest exertion during the early weeks, in them nitroglycerin may be used.

ATROPINE. Atropine in pulmonary edema is not advised. There is no good evidence that it reduces the size of the infarct or prevents arrhythmias. That atropine prevents adrenalin-induced ventricular paroxysmal tachycardia in animals is not an adequate reason to warrant its use prophylactically in the clinic. Moreover, the evidence that atropine is a coronary vasodilator in the amounts given is not conclusive. In addition it does not appear wise to increase the heart rate to the extent which would occur in securing an adequate atropine effect.

INSULIN. In a diabetic patient who is taking insulin it may be wise to delay the use of insulin for a few hours after the onset of acute coronary thrombosis in order not to run the risk of a fall in blood sugar so soon after myocardial infarction.

Complications

Shock

Sometimes with the occurrence of myocardial infarction the blood pressure falls to low levels and the patient appears to be in shock. There has been some discussion lately about the use of plasma, whole blood, or plasma and whole blood in such a situation. Most physicians who have had a wide experience in treating coronary thrombosis do not subscribe to the use of plasma. By increasing the blood volume and by drawing fluids into the blood stream, a load may be placed on the damaged heart which may precipitate acute heart failure. The use of whole blood increases the blood volume by large amounts of fluid and increases the work of the heart, although one report states that 1800 cc. plasma and 400 cc. whole blood were given in 40 minutes without the occurrence of heart failure. I have had no experience

with intra-arterial transfusions The use of oxygen and the management of the patient as described is usually effective without plasma.

I do not recommend hypertonic glucose intravenously in shock, this too increases the blood volume by drawing fluid into the blood stream and may cause acute heart failure

Norepinephrine has been used in combating shock in myocardial infarction. 2 mg (2 cc) can be given by slow infusion in 500 cc of 5 per cent glucose intravenously spread over many hours, serial blood pressures being taken as the guide to the rate of injection It elevates blood pressure and increases peripheral resistance without decreasing cardiac output and without causing cardiac arrhythmias. If this drug is not available ephedrine or neosynephrine may be used.

Frequently patients who show the picture of shock do very satisfactorily.

Heart Failure

Careful observation should be made as many as three times a day in very sick patients to detect the early signs of failure in order that it may be treated in the early stage. If acute pulmonary edema arises it is treated as described in Chapter 1 Aminophyllin 0.48 Gm intravenously, morphine, and oxygen should be used promptly I do not advise the use of hypertonic glucose intravenously. The fluid intake is restricted to 1200 or 1500 cc. and the 2.0-Gm salt diet ordered. One of the mercurial diuretics may be used intravenously if fluid accumulations or râles appear.

Whether heart failure appears acutely or comes on more slowly, digitalis is used as in other patients with cardiac decompensation. If the need for digitalis arises early in the course of the disease there are no special precautions in its use The patient is digitalized within 24 hours by either the whole leaf or digitoxin orally An intravenous preparation is recommended for faster digitalization, ouabain or lanatoside C may be used The damaged heart muscle does not appear to be particularly susceptible to abnormal rhythms or premature contractions from the administration of digitalis in therapeutic amounts However, it is best not to use this drug in the presence of ventricular premature contractions which have appeared in the course of myocardial infarction unless they are due to failure, because it may lead to ventricular paroxysmal tachycardia If digitalis becomes advisable between one week and ten days after the onset of the infarction, the drug should be given more slowly because the increased contraction of the heart muscle resulting from digitalis may result in rupture of the heart at this time Nevertheless the need for digitalis takes precedence over the possibility of this latter event The need for digitalis may be temporary, indeed critical clinical judgment may be required in deciding whether the continued use of the drug is necessary. It is usually better to try to discontinue the drug while the patient is at rest in bed in a state of compensation or to wait until mobilization is completed, in order not to introduce too many variables The progress is delayed by the occurrence of heart failure and the possibility of thromboembolic phenomena is increased Patients may, however, make a satisfactory recovery

Other details of the management of congestive heart failure are given in Chapter 1

Arrhythmias

PREMATURE CONTRACTIONS. I do not subscribe to the routine use of quinidine to prevent the occurrence of ventricular premature contractions or arrhythmias in the presence of myocardial infarction. If ventricular premature contractions occur infrequently they need cause no concern. When, however, they are frequent, they may be the forerunners of ventricular paroxysmal tachycardia. Quinidine may then be used orally in 0.4-Gm amounts three to four times a day or more frequently if it is required. Pronestyl may be effective orally in 0.25-to 0.50-Gm doses every four to six hours (p. 178). The evidence is not conclusive that papaverine gives rise to any significant coronary vasodilatation that would be useful at this time. I do not use it to prevent premature contractions.

VENTRICULAR PAROXYSMAL TACHYCARDIA. When ventricular paroxysmal tachycardia occurs immediate measures should be instituted to bring about its termination. This complication makes the prognosis less favorable. This rhythm results in marked decrease in cardiac output with further fall in blood pressure Unless it is interrupted it may lead to heart failure. Quinidine may be used by mouth or intramuscularly (pp. 176-177). It should be given in large doses without waiting to detect idiosyncrasy, and in most instances there is a favorable response. I do not think that quinidine should be used intravenously unless other measures fail. Ventricular paroxysmal tachycardia as a complication of coronary thrombosis causes concern but it is not common enough to warrant the routine use of quinidine in all patients as a prophylactic measure.

Recently I have found pronestyl effective (see p. 178 for dosage). It can be given intravenously and is effective within a few minutes, while several hours may elapse before oral or intramuscular quinidine is effective Oral pronestyl may be effective within one-half hour.

SUPRAVENTRICULAR PAROXYSMAL TACHYCARDIA AND AURICULAR FLUTTER. These are treated with adequate digitalization or other appropriate measures, as described in Chapter 5

AURICULAR FIBRILLATION. This is treated as described in Chapter 5. The ventricular rate is first retarded with digitalis. Quinidine may be necessary if the rhythm persists

HEART BLOCK. All grades up to complete block may occur when there is septal involvement; in addition to the auriculoventricular conduction defects, bundle branch block may be present. These may appear early and persist for a matter of days or they may remain permanently. There is no medication that can be used to prevent or alter these defects. If digitalis is required because of failure it is used even in the presence of high-grade block. Occasionally it is effective in preventing Adams-Stokes attacks. If complete heart block with Adams-Stokes attacks occurs, adrenalin 0.5 to 1.0 cc., 1:1000 in aqueous solution or in oil is given by hypodermic and may require repetition several times a day Even though one had just as soon not give this drug in the presence of myocardial infarction because it raises the blood pressure and also may induce ventricular rhythms, its use may be inevitable. Quinidine should not be used in the presence of conduction defects or of bundle branch block.

Embolic Phenomena

The treatment of thromboembolic phenomena in myocardial infarction has been discussed in Chapter 4

Ventricular Rupture into Pericardium

When rupture of the heart occurs into the pericardium there is nothing that can be done to alter the spontaneous course. Blood escapes into the pericardial cavity and usually leads to cardiac tamponade and a rapidly fatal outcome. If the tear through the myocardium takes a circuitous route and has a small lumen, the leak may be so slow that there is opportunity for the blood to clot, and the rent may be sealed This is more likely to occur if the patient remains very quiet.

Rupture of the Interventricular Septum

This accident is occasionally seen Careful observation of the patient may permit the diagnosis clinically When rupture occurs through the interventricular septum a systolic murmur appears over the precordium, perhaps accompanied by a systolic thrill The venous pressure suddenly rises and heart failure appears rapidly This is occasioned by the sudden shunt of blood from the left to the right ventricle through the septal opening and by the resulting change in the pressure relationships If heart failure is already present it is aggravated by this accident There is nothing specific that can be done except complete rest in bed and meeting the signs of failure as they arise.

Shoulder-Arm Syndrome

Occasionally following coronary thrombosis patients exhibit the shoulder-arm syndrome. They suffer pain, stiffness, and limitation of motion of the shoulder and arm—most frequently of the left, but occasionally of the right. It is attributed to disuse of the arm because of the pain which was present during the acute discomfort of myocardial infarction It comes on about one month after the coronary thrombosis and may persist for many months afterward. Certain patients may develop deformity of the hand resembling Dupuytren's contracture.

TREATMENT. Many forms of therapy have been employed in the past: analgesics, local heat, roentgen ray therapy, diathermy, local procaine infiltration, upper thoracic sympathetic block with procaine, and surgical thoracic sympathectomy. It has been found recently, however, in this form of shoulder disability as in bursitis, that prompt relief is achieved by the use of cortisone orally. Within 24 hours there may be prompt subsidence of pain and increased mobility of the joint.

Hiccup

Hiccup is a disagreeable symptom It is usually seen in very sick patients and may be a poor prognostic sign. The inhalation of 5 to 10 per cent carbon dioxide with oxygen may give relief. Morphine may be effective. If abdominal distention is a contributing factor it should be actively combated. I have not seen occasions in myocardial infarction when phrenicotomy was required.

Management of Patients

What to Tell Patient and When to Tell It

No illness calls for as much confidence on the part of the patient as does coronary thrombosis. The patient should accept the illness and adjust promptly to it. However, when the patient is very sick the physician's visits should appear to be prompted by interest and not by worry The patient is told enough at once to get him to agree to bed rest. If the patient is very sick he will of course be aware that he is ill and will give in readily to the suggestion of going to bed for observation This will take care of 24 hours or so, during which the physician does not wish to cause undue concern by revealing the diagnosis. The patient should be reassured and told that the use of oxygen is to "take the load off the heart." Within a few days, if he is not too sick, an explanation of his illness and what has occurred is given in simple terms, the object and the importance of complete rest at this time is described. It is much better to have the patient understand his illness and the reasons for the kind of care he is receiving and to have him adjust early to the situation, than for the physician to temporize, stretching out the bed rest by the day or week. When the patient asks about the length of time he will be kept in bed, the physician might state that it varies from patient to patient, and set an average time of six to eight weeks, adding that if it can be shortened safely this will be done Any shortening of the time when progress has been rapid will be accepted with encouragement. But the physician should not use the promise that "if all goes well" the time can be shortened because the patient will be worried that all has not gone well if there turns out to be a delay The rationale of being fed, of having bed baths, of using the bedpan, of deep breathing, and of moving his legs is explained. to spare the heart of as much exertion as possible and not to obstruct the peripheral circulation

Following the acute stage and during the last weeks of bed convalescence the physician should think about the next stage in therapy He should find out what courses are open for care of the patient after leaving the hospital If the patient has been at home during the illness, the next step in convalescence must be planned ahead of time. The patient should not be allowed to read too soon after the onset of the illness, the nurse or relatives may read to him. After the first few weeks of uncomplicated myocardial infarction the patient may turn the pages of a book as he reads from a rack or holder

Visitors

I limit visitors to one or at most two members of the immediate family in the first few days and then only for brief periods. The family is told something about the patient's illness, what may be in immediate store, and something about prognosis The family should be requested not to discuss these details with the patient. Usually the limitation on the number of visitors remains at one or two a day until toward the end of convalescence This program may then be liberalized. Weight is given to the family's appraisal of the effect that the individual visitor has on the patient with respect to raising his morale, cheering him up, or creating anxiety and irritation When it is necessary to discuss the restriction of visitors with the

patient, the point of view might be taken that as long as he has to be in hospital or in bed he may as well get the most out of it.

Patient's Routine

In the first few days of the illness when the patient is kept as quiet as possible, perhaps under the effect of morphine, sleep may be a matter of using the drug when required for pain without much attention as to whether the patient sleeps during the day or the night. As the patient improves in the course of the next few days a routine should be established. The bed bath, the enema when required, the laboratory tests, the taking of electrocardiograms should be scattered through the day so as not to tire the patient. A schedule should be organized in which the patient remains awake a good part of the day and sleeps well at night. After lunch a rest period or a nap of at least one hour should be required. The patient is not permitted to sleep too long in order not to detract from the night's sleep. Many patients who, when they are well, go to bed late, should begin the habit of going to sleep early in the evening If this routine is acquired early it may make it easier for the patient to accept a short day later on if it is necessary. For patients who are unable to sleep soundly I prescribed sodium pentobarbital 0.1 Gm. at night in order that they may have good nights and thus feel better in the daytime. Weaning from this routine can be left until later in convalescence.

Daily Physical Examination

It is a good practice to examine the patient routinely every day in order to learn how he is managing, and to detect any complications If this routine is started the patient expects it and is not concerned by it. Otherwise, if the patient has an unexpected rise in temperature or a complication arises, and the physician begins to make all kinds of examinations, the patient is troubled and knows that something has gone wrong with his progress.

The basic examination need not take long observation with respect to cyanosis, respiratory distress, venous engorgement, measurement of blood pressure and pulse, auscultation of the heart for rhythm, sounds, and pericardial friction rub, and location of the point of maximum impulse; percussion together with auscultation of lungs anteriorly and posteriorly for the presence of râles, and examination for enlargement of the liver, abdominal distention, edema, peripheral pulses, and tenderness along the veins. The patient is turned in bed, he does not sit up in bed for examination until toward the end of his stay in bed

Position in Bed

The patient lies in bed as he is most comfortable. If he is dyspneic he may be propped up to whatever level he finds satisfactory. He may be comfortable on one or two pillows. Raising the head of the bed during the day may be restful, but the patient is not permitted to sit up.

Nursing Care

Good nursing care is reflected in the ease of taking care of the patient and in his progress. This includes the bed bath, feeding the patient, insisting upon the

use of the bedpan, care of skin to prevent pressure on the skin, breathing exercises Turning of the patient frequently when sedatives are being given is necessary to prevent dependent pulmonary stasis and possibly pneumonia.

Smoking

If the patient is a smoker he should stop smoking with the onset of the attack of coronary thrombosis. In most instances I think it is best if he gives up smoking permanently. While the patient is sick he does not miss smoking. If he is alone in a room and the family or visitors do not smoke, it may be relatively easy for him to submerge the desire to smoke as he improves. The reason for this program is discussed with the patient. The physician can with profit make a point of allowing the use of some alcohol in place of tobacco, and in practice this works very well, since many patients stop smoking at this time and have no further inclination to resume the habit. The physician frequently has to temper this advice with expediency. For instance, it might be difficult to convince a very old man that it is worth the struggle to give up smoking; indeed it might not be in view of the maximal increase in longevity that might be expected from this denial. I take care to explain to the patient that we cannot prove that it has a definitely harmful effect in most instances. If the patient elects not to follow this advice after recovery, denicotinized cigarettes may be used.

Laboratory Tests

When the diagnosis is clear-cut a competent physician can treat a patient with coronary thrombosis even without laboratory tests. But in communities where these technics are available the physician can have a keener insight into what is going on and a better comprehension of the severity of the illness by their use. During the early days of the illness, when the electrocardiographic pattern may evolve slowly, *electrocardiograms* may be taken daily in order that moderate changes may not escape attention The *white blood cell count* might also be made daily. This begins to rise usually in the first 12 hours, certainly in the first day; leukocytosis persists on the average at least five days in uncomplicated, not too severe cases The *sedimentation rate* should be taken at once within the first few hours to serve as a base line and is then followed at intervals of a few days It rises within three to four days and reaches a peak in one week to ten days after the onset, in uncomplicated cases In mild cases the sedimentation rate may not change, or may be normal by the end of one week to ten days. Usually, however, there is a gradual fall to normal in one month After the peak in temperature is reached and there has been elevation with gradual fall in white blood cell count and sedimentation rate, these observations together with the electrocardiogram may be repeated at first twice a week and then once a week for the remainder of the stay in bed at home or in a hospital, and during convalescence

The foregoing data give a continuous base line to use for the detection of complications, of further extension of the lesion, or of the occurrence of new infarctions. Repeat examinations should be recorded whenever there is the suspicion of further insults to the myocardium. When digitalis is used its effect may be observed in the electrocardiogram in order to help in separating such changes from

those representing the evolution of the T waves and RS-T segmental patterns following the infarction. These data are also helpful in deciding when it is wise to mobilize the patient. For example, if the electrocardiogram is still showing marked evolutionary changes and if the sedimentation rate and white blood cell count have not fallen to normal, I prefer to keep the patient in bed beyond the one to two months' period which was planned When only the sedimentation rate remains elevated after several weeks, some other cause for this should be sought, among these would be a prostatic infection in men, pelvic disease in women, or hidden venous thromboses In a few patients the sedimentation rate remains elevated in the absence of any evident factor except the coronary thrombosis. In these the possibility of mural thrombi has to be considered After an adequate period of waiting for this single abnormality to disappear, I usually begin cautious mobilization, in some instances the sedimentation rate then falls or may remain elevated without any apparently ill consequences to the patient.

When arrhythmias appear, electrocardiograms give the exact diagnosis and permit proper treatment to be instituted. When electrocardiograms are not available, treatment should be instituted based on clinical impression

Mobilization

If the course has been uncomplicated and if all the evidence, both clinical and laboratory, points to a satisfactory convalescence, mobilization is undertaken If complications have arisen and have been met satisfactorily, if heart failure has appeared and has been alleviated, and the patient's functional capacity at rest in bed stabilized, mobilization is undertaken

In elderly patients the regimen of four to eight weeks in bed may require modification if inactivation for this length of time appears unwise because of senile changes, hypostatic pneumonia, or uremia The use of a commode instead of a bedpan may be necessary also under these circumstances Moreover, when patients are obstinate and will accept only the minimum of restrictions, modifications of this regimen must be made if the patient is to have any supervision at all. The family is apprised of the risks which are incurred with failure to comply with the optimal regimen

If the patient has been lying flat in bed the first step is the re-establishment of vasomotor balance He should be slowly propped up for a few minutes, gradually increasing the degree and the time until he is sitting up straight with back support during the last week in bed When this has been accomplished he may be propped up while eating As he progresses he may feed himself in bed one meal a day for a couple of days, then two meals a day and finally all three meals If all goes well the patient sits on the side of the bed with his feet in a chair for 15 minutes or longer, twice a day for a couple of days. All this depends on the length of time he has been in bed This restores accommodation for the dependent position to the lower extremities The patient lies down as soon as he feels fatigue rather than adhering strictly to the schedule

A day is not set ahead of time for the patient to get out of bed in order to avoid disappointing him The patient is allowed to sit up without previous notice and, if he is in a hospital, without the family being present. The presence of the

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If the course has been uncomplicated and if all the evidence, both clinical and laboratory, points to a satisfactory convalescence, mobilization is undertaken. If complications have arisen and have been met satisfactorily, if heart failure has appeared and has been alleviated, and the patient's functional capacity at rest in bed stabilized, mobilization is undertaken.

In elderly patients the regimen of four to eight weeks in bed may require modification if inactivation for this length of time appears unwise because of senile changes, hypostatic pneumonia, or uremia. The use of a commode instead of a bedpan may be necessary also under these circumstances Moreover, when patients are obstinate and will accept only the minimum of restrictions, modifications of this regimen must be made if the patient is to have any supervision at all. The family is apprised of the risks which are incurred with failure to comply with the optimal regimen

If the patient has been lying flat in bed the first step is the re-establishment of vasomotor balance. He should be slowly propped up for a few minutes, gradually increasing the degree and the time until he is sitting up straight with back support during the last week in bed. When this has been accomplished he may be propped up while eating As he progresses he may feed himself in bed one meal a day for a couple of days, then two meals a day and finally all three meals If all goes well the patient sits on the side of the bed with his feet in a chair for 15 minutes or longer, twice a day for a couple of days All this depends on the length of time he has been in bed This restores accommodation for the dependent position to the lower extremities The patient lies down as soon as he feels fatigue rather than adhering strictly to the schedule.

A day is not set ahead of time for the patient to get out of bed in order to avoid disappointing him The patient is allowed to sit up without previous notice and, if he is in a hospital, without the family being present The presence of the

family when the patient achieves this important step in convalescence increases his anxiety, excitement, and fatigue. If the patient has not been in bed too long and is not too weak, he may sit in a chair at the bedside for one-half hour—or *15 minutes in two trials—the first day. Walking is not allowed. The next day* he sits up for one-half hour in the morning and again in the afternoon, the next day, three-quarters of an hour twice a day; the next day, two hours twice a day, and following that, two and one-half hours twice a day. The accent is placed on a *gradual increase. The patient is not permitted to have a meal sitting up until the* end of this first week. During this time the other part of his regimen, such as rest after lunch, is unchanged.

After the patient is sitting up five hours daily, this is kept constant and the *patient then begins to take a few steps several times a day while sitting up in the* morning and in the afternoon. As strength of the legs returns the amount of walking around the room is increased. From this point on the amount of walking is increased more rapidly. In the hospital, lengths of a corridor may be used as *standards When the patient begins to walk he is permitted to go to the lavatory* when he is up and toward the end of this week if all has gone well, he can get up out of bed to go to the lavatory. When all of this has been accomplished the patient is ready for a tub bath or shower. During this mobilization period I keep visitors *restricted in order to avoid undue excitement*

If a patient has been in the hospital it is well, when it can be managed, to have him able to care for himself by the time he goes home. It is better if he can go home without a nurse, in order to leave the hospital atmosphere behind. How long *each patient stays in the hospital depends upon how much care and supervision* can be maintained at home. If there are stairs to manage and the patient does not wish to remain on one floor, he may remain in the hospital a few days longer in order to test climbing of stairs The first day he walks up four to five steps and then down, the next day a few more steps are added The number is increased until a flight can be managed If the patient is at home the climbing of stairs is worked out in the same way If the patient has had heart failure or if angina persists climbing stairs may not be possible at this stage.

If the patient has been in a hospital, during the first few days at home he should follow the hospital routine without any new increments, because he must adjust to being home. After this the patient sits up one hour longer daily for a week, keeping to the remainder of the routine, including going to bed early When the patient begins to go out he may go to the street the first time, next day walk part of a block and next day a slightly longer distance.

When the patient has several flights of stairs to climb there must be an appropriate delay in the patient's going out until he is able to manage the stairs During convalescence at home the patient begins to see friends and have guests for meals.

Early in the illness the patient is reassured about his future health and told that the regimen is planned with the objective of getting him back to his previous occupation As time goes on, if it appears that this goal is not possible it should not be expressed *to the patient By gradual increase in the patient's activities during* convalescence, the physician should gain a notion of what the patient's functional

capacity is going to be and have in mind what adjustments are possible in achieving some measure of this goal.

When there is a gradual progression of mobilization it is possible to stop at any level as the optimal degree of activity is reached. The early activities are the ones that it is necessary for him to be able to do if he is to manage at all on his own. If, on the other hand, a patient starts to do everything at once and begins to have symptoms or develops heart failure, not only may harm result, but also one will not know how much activity would have been possible without symptoms.

During convalescence the physician should allow ample time every week or ten days for the patient to talk and thereby provide release for tension and worries. The physician may sit at the bedside and give the patient the impression that he has ample time for whatever may be causing the patient concern.

Return to Work

In most instances I advise patients, even those who experience a mild course of myocardial infarction without complications, to remain away from work a total of four to six months. I think this plan is beneficial in the long run. A new way of earning a living or a new occupation must be recommended to some patients, if the previous one is contraindicated. Under ideal circumstances some such schedule as the following is advised, realizing that adjustments have to be made for each individual: When the patient goes back to work he goes to the office the first day for a brief period and sees fellow workers and thereby crosses this emotional hurdle, for the next few days he works one or two hours, after this he works one-half day for a few days, followed by a gradually lengthening day until he is doing a full day's work In this schedule it may be found that he can manage a full day's work All this depends on the kind of work and amount of physical and emotional effort required. The number of days for each increment will vary from patient to patient Patients who are laborers may not be able to return to the same kind of work.

The primary objective is to get the patient back to his job and economic independence Convalescence can be made the occasion for the individual to assess his work, his aims, hopes, and ambitions; to decide how many of the things he is doing are essential, which ones can be given up without altering his major work, or prime usefulness, and what activities can be severed without too much mental distress It is the common experience to have certain individuals enter their period of greatest accomplishment after coronary thrombosis, when it is made the occasion to consolidate their efforts and select judiciously the avenues for future expenditure of energy.

Exercise

Most individuals have to expend enough energy in the course of 24 hours' activity to make it unnecessary to provide any organized regimen of exercise After the patient has again been established at his work the physician, having in the meantime discovered what the patient is interested in, decides whether these extra-curricular activities are advisable and compatible with his functional capacity, in addition to carrying on the business of earning a living. I do not encourage any

activity to the point of fatigue for exercise. A patient may be able to manage nine holes of golf or perhaps eighteen on a course without hills when it is done carefully and for fun and without the drive of competition, but sudden or prolonged expenditure of energy is not wise for most patients. Tennis is for the most part too strenuous, as is swimming, unless the water is warm and the patient can always stop when fatigued. With care about fattening foods, the patient need not put on too much weight even though the amount of exercise is reduced.

A great number of patients get back to normal activity with the overexertions omitted. It is not uncommon for patients who have been of the very athletic and outdoor type to keep asking in the first months after recovery when they will be allowed to engage in this type of activity again. A few months later the patient will admit he does not wish to play tennis or climb mountains again, that in retrospect he has not enjoyed them for some time before his illness, but that he disliked giving them up and admitting he was "getting old." If the patient comes to this point of view of his own accord, he may be expected to continue with whole-hearted cooperation in maintaining his regimen.

Diet

The management of the diet during the acute illness and convalescence has been outlined. In the long-range regimen the patient should lose weight gradually if he is overweight. An attempt should be made to attain the ideal weight for the age, sex, and body build. This should be achieved without the use of thyroid extract, benzedrine, or other artificial devices. The diet should be a balanced one containing all of the essential components. Vitamin supplements may be useful. At the present time it does not appear to be wise to prescribe diets low in cholesterol and in animal and vegetable fat unless several tests have shown that the serum cholesterol and lipoproteins are significantly elevated. There is no clinical evidence that the use of choline, inositol, and other lipotropic factors will alter the course of manifest arteriosclerosis. Progress which has recently been made in the understanding of the nature and genesis of arteriosclerosis is impressive, but it has not reached the point where practical application can be made to the treatment of clinical arteriosclerosis.

Follow-up Examinations

When getting back to doing things, the patient should be encouraged to have confidence in himself. It is best not to set definite dates to do things but to add further activities without the patient having too long to think about them. Continued supervision is a safety measure to detect changes in the patient's course After convalescence he should see the physician once a week to set the following week's schedule, this interval becomes longer as the schedule can be planned further ahead. When the patient has returned to work he should be seen by his physician at first every three months, then every six months; then he should be examined at least once a year even though he feels well. At these times an electrocardiogram may be recorded and occasional two-meter roentgenograms of the heart to detect changes in size.

The patient may come through one or more attacks of coronary thrombosis in succession and find that with reasonable care about excesses he can still lead

an active, useful life. On the other hand, some restriction with some alteration of the work pattern may also be required if the patient is to be without symptoms and remain within his functional capacity. Then there are those patients who have symptoms and experience complications even after curtailment of activity. There may be varying degrees of precordial pain on effort or emotion or manifestations of decrease in cardiac efficiency such as breathlessness, palpitation, and varying degrees of subjective and objective manifestations of heart failure All these will require continued treatment and indefinite supervision. Many patients who have had angina for some time before the attack of coronary thrombosis may be free of angina afterward.

The physician must not be discouraged but must face the patient with optimism and encourage him to keep his activities within what he is able to do comfortably. Patients become adept in the way to get around excessive demands on their heart. Once a patient accommodates mentally to these restrictions the management is much easier and there is no inward struggle when he is confronted with the things which are contraindicated

Sexual Intercourse

One of the first questions which the patients ask during convalescence is how soon they may have sexual intercourse In order to answer this helpfully some background of the patient's sexual habits is needed: the usual frequency, the time taken in precoital play, the time to reach climax, the demands of the partner. The physician should ascertain whether the patient had any symptoms during intercourse before the coronary thrombosis, which may have been related to coronary insufficiency With satisfactory recovery from coronary thrombosis further celibacy of around two months after the patient has made the adjustment to being home may be adequate This, however, depends on the emotional response of the patient. Advice is given about shortening the precoital play and the whole act during the first sexual intercourse after myocardial infarction. In this discussion with the patient no apprehension of the consequences of intercourse should be aroused

CORONARY EMBOLISM

Although coronary embolism is uncommon it must be kept in mind. It occurs most frequently as an embolic manifestation in subacute bacterial endocarditis, rarely the embolus is from an atherosclerotic plaque in a setting of arteriosclerotic heart disease. The electrocardiographic picture may give evidence of anterior apex or of posterior base involvement. I have seen it in a young lad 12 years of age after a ruptured gangrenous appendix The symptoms and course of acute coronary occlusion due to coronary embolism may be similar to those due to coronary thrombosis. In most instances of coronary embolism coronary vessels which have been essentially normal are suddenly occluded by the embolus The neighboring vessels being approximately normal, the opportunity for attaining an adequate collateral circulation is maximal.

With respect to rest and allowing adequate time for healing, the patient is treated as is any patient with myocardial infarction The implications, however, are different from those when coronary occlusion results from coronary thrombosis in

patients with coronary artery disease. For instance, with cure of the subacute bacterial endocarditis, and recovery and healing of the myocardial infarction resulting from coronary embolism, the functional capacity may be restored to its former level When coronary embolism occurs in subacute bacterial endocarditis anticoagulants are not recommended.

CORONARY THROMBOSIS IN YOUNG PEOPLE

The reports of coronary thrombosis in subjects in the younger age ... increasing This is probably due to ...

... found to be due to ... vessels by arter...

ANEURYSM OF LEFT VENTRICLE

Following myocardial infarction there may be adequate replacement with scar tissue so that a strong ventricular wall results. On the other hand, the wall may become weakened and thin and a ventricular aneurysm result. Ventricular aneurysm is recognized in the x-ray photograph of the heart as a bulge It is demonstrated best on fluoroscopic examination and on roentgenkymograms, a paradoxical movement of this area of ventricular wall may be seen During cardiac systole the heart shadow in this area moves outward rather than inward. In healing of myocardial infarction with or without aneurysmal dilatation, myomalacia may result which may be demonstrated in x-ray photographs of the heart A ventricular aneurysm may be discovered without any preceding clinical history of coronary occlusion. There may be no symptoms or change in functional capacity of the heart in the presence of a ventricular aneurysm When heart failure occurs it is treated in the appropriate manner; such patients are warned against sudden exertions which may lead to rupture.

CORONARY THROMBOSIS AND HIATUS HERNIA

Only after the course in suspected coronary thrombosis fails to follow the expected pattern is it justified to subject the patient to x-rays for detection of hiatus hernia as an alternative to the diagnosis of coronary thrombosis

SUMMARY

With proper care myocardial infarction may be followed by complete recovery with re-establishment of a good functional capacity The patient may be permitted to lead an essentially normal life afterward. Even the severe attacks may follow this

same pattern, except that a longer time is required for the attainment of recovery and for return to activity. At the opposite extreme, which is fortunately not the most common pattern, are those cases in which even though the patient survives the initial acute coronary thrombosis, the damage is so marked and the organ has its functional capacity so greatly diminished that the patient may be totally incapacitated because of a narrow margin of cardiac reserve. In between these are all gradations of residual effects—from those with occasional angina to those with more persistent pain; from those with slight dyspnea on exertion to those with frank cardiac failure. There are patients who experience a single attack and thereafter are free of further coronary episodes. There are those who experience several infarctions in close succession or over a period of years. Damage may be so extensive that survival is a matter of minutes, or there may be mural thrombi with embolization extending over several weeks, there may be cardiac rupture at the end of a week or ten days, or there may be a progressive downhill course with death some weeks later. But these last complications do not form the most common pattern With prompt recognition of acute coronary thrombosis and institution of proper care, the majority of the patients have the more satisfactory course.

Lay people hear a great deal about coronary thrombosis, for the most part on the gloomy side. When a patient is stricken with myocardial infarction he should be promptly reassured in order to balance the hidden worry. It is a disease in which prompt and adequate rest insures a better opportunity for healing of the damaged area and forestalls overstraining a damaged myocardium. Patients may use the episode to reassess their life accomplishments and future hopes and, by freeing themselves of useless activities, enter upon one of the most productive and satisfying periods of their careers

Treatment is for the most part symptomatic along with proper management of complications which may arise At present there are no drugs which promote healing or increase the collateral circulation Recently anticoagulants have been advocated in order to prevent extension of the coronary thrombosis, the formation of mural thrombi, and thrombophlebitis with rest in bed and the resulting danger of emboli At the present time I do not think that the anticoagulant regimen should be used routinely in all patients who have suffered acute coronary thrombosis. Its use would not be indicated in mild infarctions which from clinical evidence do not appear to be extensive. When anticoagulants are contemplated, the contraindications should be carefully explored. Anticoagulants should be reserved for patients who have had severe extensive infarctions from which mural thrombi might form, and in whom extension of the thrombosis might occur and heart failure develop, for those in whom congestive heart failure occurs early, for those with repeated thromboses or extensions of older ones, for those who have had previous severe infarctions, for those who develop cardiac irregularities which predispose to mural thrombi; and for patients who suffer thrombophlebitis or embolic phenomena There is at present no basis for the continued use of anticoagulants after the immediate need for them has passed, and no basis for their prolonged and continued use in patients to prevent coronary thrombosis.

The early recognition of myocardial infarction is necessary. The clinical picture should take precedence over laboratory findings in arriving at a diagnosis. The

patients with coronary artery disease. For instance, with cure of the subacute bacterial endocarditis, and recovery and healing of the myocardial infarction resulting from coronary embolism, the functional capacity may be restored to its former level When coronary embolism occurs in subacute bacterial endocarditis anticoagulants are not recommended.

CORONARY THROMBOSIS IN YOUNG PEOPLE

The reports of coronary thrombosis in subjects in the younger age group are increasing This is probably due to a clearer recognition of the symptoms and to increased skill in diagnosis Many of the fatal instances of acute coronary thrombosis resulting in infarction in young subjects have been found to be due to localized narrowing of coronary vessels by arteriosclerosis Xanthomatosis may be the cause of coronary thrombosis in younger individuals.

The treatment of these patients does not differ from that accorded other subjects. Even when there is recovery from an attack, the prognosis must be guarded because there may be other localized areas of arteriosclerosis

ANEURYSM OF LEFT VENTRICLE

Following myocardial infarction there may be adequate replacement with scar tissue so that a strong ventricular wall results. On the other hand, the wall may become weakened and thin and a ventricular aneurysm result. Ventricular aneurysm is recognized in the x-ray photograph of the heart as a bulge. It is demonstrated best on fluoroscopic examination and on roentgenkymograms, a paradoxical movement of this area of ventricular wall may be seen During cardiac systole the heart shadow in this area moves outward rather than inward. In healing of myocardial infarction with or without aneurysmal dilatation, myomalacia may result which may be demonstrated in x ray photographs of the heart. A ventricular aneurysm may be discovered without any preceding clinical history of coronary occlusion. There may be no symptoms or change in functional capacity of the heart in the presence of a ventricular aneurysm When heart failure occurs it is treated in the appropriate manner, such patients are warned against sudden exertions which may lead to rupture.

CORONARY THROMBOSIS AND HIATUS HERNIA

Only after the course in suspected coronary thrombosis fails to follow the expected pattern is it justified to subject the patient to x-rays for detection of hiatus hernia as an alternative to the diagnosis of coronary thrombosis.

SUMMARY

With proper care myocardial infarction may be followed by complete recovery with re-establishment of a good functional capacity. The patient may be permitted to lead an essentially normal life afterward. Even the severe attacks may follow this

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electrocardiographic technic provides a method for localization and for giving a fair estimate of the extent of the damage in most patients. It is an arresting fact that a disease which has been recognized clinically for a matter of only 40 years, as a result of Herrick's classic description, is one which our medical students and internes can diagnose with a fair degree of accuracy. Moreover, it turns out to be the major cause for concern for a large part of the population turning 40.

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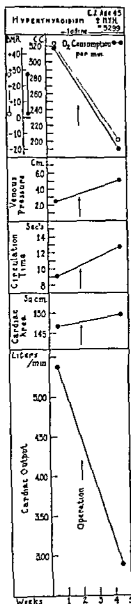


Fig 40.

Data Relating to a Woman 45 Years of Age Suffering from Graves' Disease. Basal metabolic rate was elevated, circulation time short, and cardiac output increased Iodine was given and thyroidectomy was carried out Two and one half weeks after operation basal metabolic rate had decreased, circulation time had increased, and cardiac output had decreased The values were within normal limits

CHAPTER 14

The Heart in Hyperthyroidism

PATHOLOGIC PHYSIOLOGY

Hyperthyroidism, or Graves' disease, implies an increased activity of the thyroid gland, causing increased amounts of the thyroid hormone to enter the circulating blood This hyperactivity may be a consequence of hyperplasia of the gland as a whole or of one or more lobes of the gland, or it may result from nodular enlargement. The elaboration of larger amounts of thyroid hormone increases the rate of oxidation of the tissues, a change which is reflected in the basal metabolic rate

The dynamics of the circulation are altered in Graves' disease The basal metabolic rate is increased. The arteriovenous oxygen difference is decreased The circulation time is short, indicating increased velocity of blood flow The cardiac output per minute increases greatly (Fig 40), studies indicate that the cardiac output is speeded up even above the level required by the augmented oxygen need. As a result of the increased demand on the heart, dilatation may occur, and late in the disease there may be hypertrophy

Heart failure in young individuals with hyperthyroidism is relatively uncommon in the presence of a normal rhythm, it occurs more frequently in the older group whose cardiac reserve has been diminished by arteriosclerotic changes in the coronary vessels or myocardial alterations with age. Congestive heart failure may appear with normal rhythm, but is more sudden in its appearance and progressive after the appearance of *auricular fibrillation* or *auricular flutter*, although these irregularities are not invariable precursors of decompensation. The ventricular rate may be rapid before the exhibition of digitalis when auricular fibrillation or flutter occurs *Patients with coronary artery disease may have angina because of the increase* of the basal metabolic rate in Graves' disease.

Although the circulation time decreases and the cardiac output diminishes after the onset of heart failure, both measurements may still remain above normal. They are out of proportion to what would be expected in cardiac decompensation of this degree if failure were the result of some other type of heart disease.

extent. They think that sweating is so common and profuse that strict limitation of fluids may cause discomfort. The individual patient's requirements should be considered.

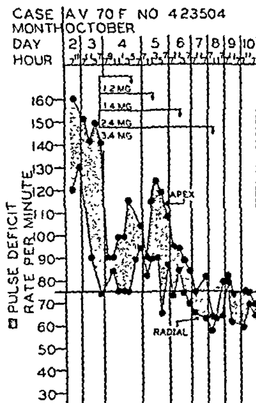


Fig 41.

Effect of Digitalization with Digitoxin in a Woman 70 Years of Age Suffering from Hyperthyroidism Patient had auricular fibrillation. Her weight was 45.3 Kg It is apparent that adequate slowing of ventricular rate to 70 per minute and reduction of pulse deficit was achieved on digitalization, but that more than the average amount was necessary A total of 3.4 mg in ninety-six hours was required Allowing for average excretion over this time of 0.15 mg × 4 or 0.6 mg., we arrive at 2.8 mg, which would probably have been required to slow the ventricular rate to 70 per minute if it had been given in twenty-four hours It is apparent that 1.2 mg was inadequate, as was 1.4 mg and also 2.4 mg It is recalled that the average amount required for digitalization of this drug is 1.8 to 2.0 mg On October 4, 1945 the basal metabolic rate was plus 53 per cent

Antithyroid medication was withheld until the effect of digitalis had been ascertained This figure demonstrates that the ventricular rate in the presence of auricular fibrillation in certain hyperthyroid patients may be satisfactorily retarded with digitalis

Urine Output

The urine output should be measured if the patient is in the hospital or facilities are available. This gives an objective guide to the amount of diuresis (see p. 22).

Weight

The patient may be weighed daily if heart failure is not too advanced. Early in the treatment the body weight tends to decline with the loss of edema fluid.

CLINICAL MANIFESTATIONS

The manifestations of congestive heart failure in hyperthyroidism are similar to those in other varieties of cardiac decompensation· dyspnea, orthopnea, venous engorgement, râles, pleural effusion, enlargement of the liver, ascites, and edema, in varying degrees and combinations.

Even after the appearance of serious decompensation, the condition may be reversible, with disappearance of auricular fibrillation, heart failure, and all evidence of cardiac incompetence There is no evidence—microscopic or otherwise—that hyperthyroidism induces specific changes in the heart muscle.

TREATMENT

Treatment of the Heart Failure

The essential aim in the treatment of heart failure caused by hyperthyroidism is to lower the basal metabolic rate as rapidly as possible. Drugs directed toward this end should be employed promptly. Because there is delay in the action of the antithyroid drugs (the thiouracils and iodine) their early exhibition is essential *They should be used simultaneously with the other measures to combat heart failure.* As we have indicated, patients usually respond well not only to treatment of the hyperthyroidism per se, but also to the treatment of the associated cardiac decompensation. In many patients the medical treatment may be regarded as preparation for thyroidectomy.

Bed Rest

The patient should be at rest in bed Patients who are easily disturbed should be in a room alone. Other patients do very well in a ward and may be quieter and more relaxed than when in a private room.

Sedation

Phenobarbital (16 mg) may be given four times a day to promote relaxation and quiet.

Diet

A low salt diet is given. This may be of high caloric content if the patient can cope with it despite the heart failure. Thiamine and brewers' yeast should be added to the diet. The requirements of the vitamin B components are augmented because of the increased metabolic rate.

Fluid Intake

It is my practice to limit the fluid intake to 1200 to 1500 cc. daily. If the patient sweats it may be increased to 1800 cc. I have not observed ill effects from limiting the fluids; the signs and symptoms of heart failure are dissipated more rapidly. Other observers, however, think that the fluids should not be restricted to this

ization until the opportune time for attempting conversion with quinidine is reached (p. 332).

In some instances auricular fibrillation or auricular flutter may be present without signs of heart failure. When this is the case digitalization is carried out in the manner already described and the same policy is followed with respect to avoiding attempts to induce reversion of the rhythm to normal until the thyroid status has become stabilized.

Diuretics

Mercuzanthin, thiomerin, mercuhydrin, or salyrgan-theophylline may be given if necessary to promote diuresis They are usually given in 2-cc amounts at three-day intervals intravenously, but may be given intramuscularly. Thiomerin may be given subcutaneously (see p 39)

Ammonium chloride 1.0 Gm. three to four times daily may be required to enhance the diuretic effect of the mercurial drug.

Treatment of the Hyperthyroidism

Iodine

The patient is given syrup of hydriodic acid 1.0 cc. or Lugol's solution 10 minims, daily. The effect of the iodine becomes apparent within a few days and is at a maximum ten to fourteen days after the drug has been started.

6n Propylthiouracil

The average dosage of this drug is 50 mg. four to five times a day. Individual requirements, however, vary greatly Some patients may become myxedematous on as little as 50 mg. a day It has supplanted thiouracil as an antithyroid drug. It blocks the synthesis of the thyroid hormone Few serious toxic effects have been recorded from its use. Its effect is slower in the presence of large nodular goiters and in patients who have taken iodine before. The effect of this drug may be striking within a week or ten days. The rate of improvement after beginning its use varies greatly, and the optimal effect may take place in one or two months

Judgment concerning the action of antithyroid drugs can perhaps be best formed when the level of cholesterol in the blood is known Whenever possible this should be determined at the time treatment is started As the drug becomes effective the cholesterol increases and the basal metabolic rate falls The white blood cell count should also be carefully observed Any adverse change in the patient's increasing sense of well-being as the basal metabolic rate falls and as the symptoms of the disease ebb should be the occasion for temporarily discontinuing the drug until the situation has been clarified

The dosage of propylthiouracil is decreased to 25 to 50 mg or less daily as the normal state is attained The maintenance dosage varies as greatly as does the initial requirement

The management of the patient during propylthiouracil therapy has been easy compared with the use of thiouracil However, the exact place of this drug in the treatment of hyperthyroidism has not been formulated. At present it appears possible to carry patients indefinitely on the drug in apparently normal states,

However, as measures to reduce the basal metabolic rate become effective the body weight has a tendency to increase. The weight may remain stationary as the two effects balance each other, and with continued improvement finally increase, owing not to water retention but to tissue gain.

Pulse Rate

If the patient has auricular fibrillation or flutter, apical and radial rates are counted every four hours while awake, or oftener as indicated. The pulse rate is recorded every four hours if normal rhythm prevails. Sleeping pulse rates—as they are not distorted by overactivity—may provide a more accurate notion of the rise in heart rate that is due to the increased basal metabolic rate.

Digitalization

The patient is treated with the whole digitalis leaf or digitoxin by mouth over a 24-hour period, or more rapidly by the use of other digitalis preparations if there is urgency (see Chapters 1, 3, and 5) The pattern of digitalization does not differ from that used in other patients with heart failure, with the following exception· It may be found that as much as 3 0 Gm. of whole leaf or 3.0 mg of digitoxin in 24 hours are required to slow the ventricular rate in auricular fibrillation when the basal metabolic rate is elevated in hyperthyroidism (Fig. 41). Moreover the maintenance amounts may be more than are required when auricular fibrillation is associated with other types of heart disease. The amount required may approach the average amounts mentioned above after the use of antithyroid drugs has lowered the basal metabolic rate When auricular fibrillation is present it may not be possible to slow the ventricular rate to the optimum of 75 or even 80 or 90 per minute even though the large amounts which have been mentioned are given. In certain patients reversion to normal rhythm may occur with the exhibition of digitalis.

The amount of digitalis may also have to be increased to reduce the ventricular rate when auricular flutter is present Slowing in these cases is achieved by increasing the degree of auriculoventricular block. Hyperthyroid patients may not become nauseated so easily on these large amounts of digitalis as patients with normal basal metabolic rates.

Usually digitalis does not significantly decrease the heart rate when sinus tachycardia is present. It is to be expected, however, that the heart rate will be slowed as the specific antithyroid medication becomes effective. The ventricular rate will then slow more satisfactorily on the same maintenance amounts of digitalis.

Conversion of auricular fibrillation or auricular flutter to normal sinus mechanism is not attempted at this stage of therapy, but is reserved until the basal metabolic rate has been reduced to normal levels by medication or by surgery, and opportunity has been afforded for spontaneous reversion to normal rhythm (see p 332). If spontaneous reversion does occur the drug is continued until the thyroid status is satisfactory and there is no further indication for its use because of heart failure After these maintenance doses have been discontinued, and as the drug is excreted, the patient should be observed for recurrence of decompensation If spontaneous reversion does not occur maintenance doses of digitalis are continued after digital-

hyperthyroidism has not yet been accurately defined. It should be employed only by those few who are experienced in the use of radioactive drugs. The basal metabolic rate can be lowered and patients relieved of symptoms by iodine administered in this form. It fact, it now appears that radioactive iodine may represent the safest, simplest, and surest way of terminating the thyrotoxic state. It may be useful in the older patient in whom for one reason or another surgery is not advisable. It also finds a place in the care of patients who have failed to remain in a remission after prolonged treatment with propylthiouracil, who have had reactions from the thiouracils, or who have had thyroidectomies. It is at present invaluable in the control of patients with heart failure who are regarded as serious operative risks. On the other hand, for patients with severe cardiac failure in whom a more rapid effect is required the use of propylthiouracil and iodine might be the drugs of first choice.

It has several drawbacks. In the first place the exact dosage for each patient cannot yet be predicted. If an insufficient amount is given at first additional amounts can be given later, but if the optimal dose is exceeded the changes are irreversible. In the second place eight to twelve weeks elapse before the maximal effect has been secured In the third place it is not known whether its use will in later years give rise to carcinoma of the thyroid gland, although this appears remote to those who have had experience with this form of therapy. When I^{131} is administered the available thyroid hormone is released, so that the patient's symptoms may be temporarily exaggerated. To prevent this 6n propylthiouracil may be given before I^{131} is used, in order to try to deplete the gland of thyroid extract before radioactive iodine is used. It should, however, be discontinued 48 hours before giving I^{131} It may not be safe to use radioactive iodine until some months after intravenous pyelograms or gallbladder visualization because of the storage in the body of the complex iodine compounds used in these tests

USE IN CHRONIC CONGESTIVE HEART FAILURE Blumgart and associates have reported on the use of radioactive iodine in the treatment of intractable congestive heart failure and of angina The rationale for its use is the same as for the use of propylthiouracil in cardiac decompensation. Patients with congestive heart failure experienced less benefit than did patients with angina who were similarly treated Some patients, however, exhibited striking improvement with the induction of the myxedematous state The use of this procedure in patients with heart failure is similar to that described for patients with angina (p. 291). Only patients who have failed to respond to all other measures for the relief of congestive heart failure should be considered for this form of therapy.

Thyroidectomy

In most instances patients become free of heart failure by the measures which have just been described The basal metabolic rate falls under the influence of antithyroid drugs and may attain a satisfactory level. The decision may be made to carry the patient along on propylthiouracil, on the other hand thyroidectomy may be indicated. With appropriate preoperative and postoperative care and skillful surgery, patients who have had heart failure sustain thyroidectomy satisfactorily.

maintaining the basal metabolic rate around the optimal level, without symptoms and with a minimum of observation. In certain patients remissions are sustained even after the drug has been discontinued.

After restoration of a normal basal metabolic rate propylthiouracil may be discontinued in a fair number of patients. A prolonged remission may be expected in about half the patients if the drug is discontinued after six months' treatment. It may be necessary to readjust dosage from time to time on occasions of stress.

Having restored the patient to a state of compensation, and reduced the basal metabolic rate to normal levels with antithyroid drugs, the question next arises of the further treatment of the patient and the advisability of thyroidectomy. The present medical methods make it possible to carry out surgery under the optimal conditions so that the operation becomes possible for most patients. Some patients can be more conveniently protected by thyroidectomy because of the frequent checks which are required when propylthiouracil is used. Although cardiac involvement is an indication for surgery, there may be a few patients with heart disease to whom it is best not to subject the additional hazard of the surgical procedure of thyroidectomy at a certain stage in the medical management (see Radioactive Iodine, below) If a satisfactory level of basal metabolic rate can be maintained in these patients the continued use of propylthiouracil may be the procedure of choice until such time as surgical thyroidectomy can be carried out. The drug offers a means of treatment in those patients who refuse surgery or in whom hyperthyroidism has recurred after one or more thyroidectomies. It offers a means of treatment in aged individuals in whom operative treatment might well be avoided.

USE IN CHRONIC CONGESTIVE HEART FAILURE. The basal metabolic rate may be increased in congestive heart failure of the various types even though thyrotoxicosis is not a factor, and may remain elevated after the restoration of compensation. The provision of this added amount of oxygen places a burden on the heart which may make the difference between moderate or reduced activity of the patient. The basal metabolic rate may be reduced in certain of these patients to or slightly below the normal level by the use of propylthiouracil. Patients thus treated are more comfortable at rest; the ventricular rate is slower on the same ration dose of digitalis, and a higher level of activity of the patient is possible. It is recalled that many months may elapse before reduction in basal metabolic rate and improvement are recorded when the drug is given to euthyroid individuals. Propylthiouracil does not affect the preformed thyroid hormone, but blocks the formation of more. Enough hormone may be stored to last for some time.

Radioactive Iodine (I^{131})

The use of radioactive iodine followed the observation that roentgen irradiation of the thyroid gland in hyperthyroidism frequently provided benefit. Failures resulted because the dosage was not high enough. Since iodine collects in the thyroid gland, by the use of radioactive iodine a high degree of radiation is planted directly in the cells which it is desired to irradiate.

The place of this isotope—which is not generally available—in the treatment of

hyperthyroidism has not yet been accurately defined. It should be employed only by those few who are experienced in the use of radioactive drugs. The basal metabolic rate can be lowered and patients relieved of symptoms by iodine administered in this form. It fact, it now appears that radioactive iodine may represent the safest, simplest, and surest way of terminating the thyrotoxic state. It may be useful in the older patient in whom for one reason or another surgery is not advisable. It also finds a place in the care of patients who have failed to remain in a remission after prolonged treatment with propylthiouracil, who have had reactions from the thiouracils, or who have had thyroidectomies. It is at present invaluable in the control of patients with heart failure who are regarded as serious operative risks On the other hand, for patients with severe cardiac failure in whom a more rapid effect is required the use of propylthiouracil and iodine might be the drugs of first choice.

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The operation may be done in two stages, at an interval of a week to ten days. It can be carried out under local anesthesia in suitable patients if there is need, or under ether anesthesia with oxygen if necessary. Careful supervision of the liquid intake during and after operation should be maintained in order not to overload the circulation with fluids. Mobilization is slower than would ordinarily be the case in order not to embarrass the heart which has recently been in failure.

UNRECOGNIZED HYPERTHYROIDISM AS A CAUSE OF CONGESTIVE HEART FAILURE

Patients with advanced heart failure in whom the common causes of heart failure are not apparent or whose auricular fibrillation is resistant to digitalization should be suspected of having hyperthyroidism and appropriate studies carried out. If these patients are too ill for a satisfactory basal metabolic rate to be obtained and if oxygen therapy is required I think that hyperthroidism might be assumed temporarily without running the risk of waiting for laboratory substantiation; iodine and propylthiouracil may be given a therapeutic trial at once.

TREATMENT OF PERSISTENT AURICULAR FIBRILLATION AND AURICULAR FLUTTER

If auricular fibrillation or auricular flutter in the presence or absence of heart failure has persisted after digitalization and the satisfactory reduction of basal metabolic rate under propylthiouracil and iodine, or thyroidectomy, it is my practice to continue to use digitalis for several weeks to afford an opportunity for spontaneous reversion to normal rhythm In a large number of patients restoration of normal rhythm occurs spontaneously when given this opportunity When reversion occurs the drug is discontinued if there is no further indication for it In some instances, however, the abnormal rhythm persists. The use of quinidine to obtain reversion to normal rhythm should then be considered. If there are no contraindications the patient is put at rest in bed and quinidine is given in the usual manner. If the patient has had heart failure for some time before treatment of the hyperthyroidism the auricles may contain mural thrombi, and embolization may take place with reversion to normal sinus mechanism. Thrombi may be liberated when reversion to normal rhythm occurs spontaneously but this complication is more disturbing when it follows a drug given for therapeutic purposes. If auricular fibrillation has been of long duration heparin or dicumarol might be used beforehand to decrease the likelihood of this accident (see Chapter 4).

Restoration of normal rhythm occurs easily and permanently with quinidine in some patients, but in others it is of short duration, and in the case of auricular flutter the irregularity may stubbornly resist efforts of conversion to normal rhythm even with large amounts of quinidine. After two or three trials the use of quinidine is abandoned and further efforts are not made to terminate either the auricular fibrillation or auricular flutter. Under these circumstances the use of digitalis is continued.

ONSET OF HYPERTHYROIDISM IN PATIENTS WITH RHEUMATIC HEART DISEASE

When a patient with rheumatic heart disease who is compensated and carrying on satisfactorily under his regimen shows increasing signs of failure on the same medication, one should suspect not only the recurrence of rheumatic infection but also the onset of thyrotoxicosis, especially (1) if the patient has suffered from heart failure before and up to this time has been maintained in a compensated state on a regimen of digitalis, low fluid intake, low salt diet, and mercurial diuretics; (2) if he has auricular fibrillation and the usual amounts of digitalis he has been requiring for maintenance now no longer keep the ventricular rate slow; and finally (3) if, in the last complication, an increased ration of digitalis fails to achieve adequate slowing. On inquiry and examination the onset of other symptoms and signs of hyperthyroidism may be elicited, namely intolerance to heat and the presence of a palpable gland

There are occasions when a patient with rheumatic heart disease and heart failure, seen for the first time, does not respond satisfactorily to the usual therapeutic measures with evidence of a ventricular rate refractory to digitalis. Under these circumstances the diagnosis of concurrent hyperthyroidism should be considered and the usual tests carried out

The same remarks also apply to the onset of hyperthyroidism in patients who have other etiologic types of heart disease especially those in the arteriosclerotic rubric

This group of patients may recover from heart failure with the institution of bed rest and of other measures, but the recovery may not be so complete as it should be and the heart rate may remain rapid When the patient is in the best possible state the basal metabolic rate may remain slightly increased, perhaps to plus 20 per cent The slowing of the basal metabolic rate to zero or to minus 10 per cent would represent a tremendous saving in the energy required by the heart to maintain an adequate circulation The achievement of this may represent the difference in the patient's life between almost no activity and moderate activity. If the existence of hyperthyroidism is established, treatment as described above may give subjective improvement within a week to ten days Patients acquire a feeling of relaxation and inward quietude

Hyperthyroidism may be slightly more frequent in patients with rheumatic heart disease than in patients of the other common groups, such as the arteriosclerotic, hypertensive, and congenital rubrics This is probably to be attributed to the natural incidence of rheumatic heart disease and hyperthyroidism in the same age group

THYROID CRISIS

In the course of severe Graves' disease with a high basal metabolic rate and marked overactivity, a sudden emotional upset or acute infection may precipitate thyroid crisis The manipulation of the gland at operation may induce the crisis,

in which it appears usually four to sixteen hours after operation. Crises are thought to be due to the release of large amounts of thyroid hormone into the circulation, causing hyperpyrexia, extreme tachycardia, sweating, weakness, vomiting, and fall in blood pressure. It occurs most frequently in emaciated patients with severe disease This complication is cause for grave concern since death frequently results. The presence of a severe complicating disease, such as heart disease with failure, may exert an unfavorable influence on recovery from the thyroid crisis.

The best way to treat thyroid crisis is to prevent it. With the use of the newer antithyroid drugs patients can usually be prepared more satisfactorily for surgery so that thyroid crisis occurs less commonly. When symptoms of thyroid crisis appear, the patient should be given oxygen by tent, mask, or intranasally. Efforts should be made to control hyperpyrexia by hydrotherapy. An infusion containing dextrose and thiamine is given to protect the liver Propylthiouracil 300 mg. is given with the idea of suppressing the manufacture of new thyroid hormone in the gland. However, since its effect is delayed it cannot be expected to be of much benefit during the crisis. One hour later 2.0 cc. of a saturated solution of potassium iodide is given, even though it may also act too slowly in the inhibition of the release of thyroid hormone from the thyroid gland to exert great usefulness in the crisis. Sodium iodide 1.0 Gm (10 cc of a 10 per cent solution) has been given intravenously to secure rapid absorption. Propylthiouracil and iodine are continued simultaneously thereafter. If the fall in blood pressure is precipitous, plasma infusions and blood transfusions may be required Penicillin may be used to combat infection which may arise during the crisis Adrenal exhaustion has been reported, because of this whole adrenal cortical extract has been given to a few patients. Vitamin K may be given to reduce the prolongation of the prothrombin time which may be present as evidence of liver damage.

Thyroid crisis is a serious and alarming complication and all efforts should be made to prevent its occurrence.

SUMMARY

The cardiac manifestations of hyperthyroidism include congestive heart failure in which the cardiac rhythm may be normal sinus mechanism, and auricular fibrillation or auricular flutter as the most common irregularities. On the other hand auricular fibrillation or flutter may occur without heart failure. Angina pectoris may occur in older patients in the coronary artery age group. Heart failure is treated as in other patients with cardiac decompensation, together with the use of iodine and [illegible] measures compensation should be restored and the [illegible] or attain a normal level. Thyroidectomy may thei [illegible] ar fibrillation or auricular flutter are present the use of digitalis is continued. Attempts are not made to restore normal rhythm with quinidine until an adequate opportunity is presented for reversion to occur spontaneously after the restoration of normal basal metabolic rate by medical or surgical means. If reversion does not occur, and the patient is free of failure, quinidine may be used when there are no contraindications By skillful pooling of medical and surgical care, patients with advanced heart failure are restored to normal activity commensurate with their age and with any concomitant handicaps.

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CHAPTER 15

Myxedema (Hypothyroidism)

PATHOLOGY

There is still controversy over whether hypothyroidism per se is a cause of cardiac symptoms or cardiac disease. There is a general feeling that myxedema does not induce any characteristic myocardial lesion and that the incidence of coronary artery sclerosis in these patients is of the degree expected for their age group. There are data, however, which indicate that myocardial changes do occur. For instance, in the case reported by Foster and Barr, the heart muscle showed replacement of the central two-thirds or more of many cells by vacuoles containing clear or slightly granular basophilic material. The sarcoplasm but not the sarcolemma was involved These areas were scattered throughout the myocardium but did not involve all the cells The cells were swollen to twice the normal size. In longitudinal section the basophilic areas varied in length. There was loss of smooth muscle cells and collagen throughout the medial layer of the wall of the aorta The spaces formed by this loss were filled with a basophilic material resembling that seen in the vacuolated areas in the heart muscle cells. In a few areas there were small cysts filled with this material. The changes in the aorta resembled those described by Erdheim as idiopathic cystic medial necrosis.

It is apparent that there is a morphologic basis for functional disturbance of the heart in myxedema since it may be the seat not only of histologic changes but also of an increase in interstitial fluid. Moreover, the high level of the serum cholesterol which prevails in myxedema may bear a relation to the arteriosclerotic changes which are common in these patients. It has already been pointed out that the arteriosclerosis associated with myxedema has been attributed to the natural incidence of this degenerative process in the age group in which most of these patients fall. The medial necrosis with vacuolization which has been reported, however, is different from the usual changes seen in arteriosclerosis.

CLINICAL MANIFESTATIONS

It is not surprising that the well-developed picture of myxedema has cardiac manifestations and that cardiac complications occur. The myxedematous state is accompanied by the presence of fluid in the serous cavities: pericardial, peritoneal,

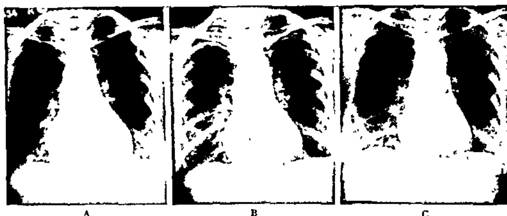
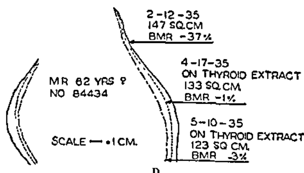


Fig 42

Roentgenograms of the Chest of a Woman 62 Years of Age, to Demonstrate Enlargement of the Cardiac Shadow in the Myxedematous State, and Progressive Decrease in Size of the Heart with Administration of Thyroid Extract.

A, February 12, 1935, when the basal metabolic rate was −37 per cent, before thyroid extract was given *B*, April 17, 1935, after the basal metabolic rate had risen to −1 per cent on the administration of thyroid extract *C* shows the size of the heart on May 10, 1935 when the basal metabolic rate was −3 per cent *D* represents outline of the heart traced from x ray photographs *A*, *B*, and *C* on thin paper and superimposed in order to demonstrate the progressive decrease in size. (Stewart, H J, Deitrick, J E, and Crane, N F Studies of the circulation in patients suffering from spontaneous myxedema *J Clin Investigation* 17 237, 1938)



and pleural The so-called "myxedema heart" has been characterized clinically by enlargement of the cardiac shadow in the x-ray (Fig 42), which is reversible on treatment with thyroid extract This enlargement is thought by some investigators to be due entirely to pericardial effusion which may be demonstrated by pericardial tap and by visualization of the cardiac chambers On the other hand the shape of the heart on fluoroscopic examination and the absence of increase in venous

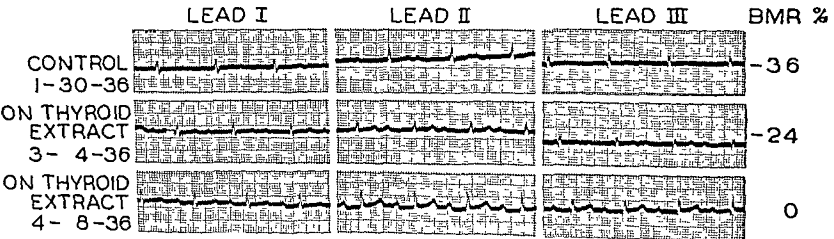


Fig 43.

Electrocardiograms on a Woman 26 Years of Age to Illustrate Changes Seen in Myxedema January 30, 1936, low amplitude of the QRS complexes and T waves and the P-R time greatly prolonged, being 0.56 second in Lead II Basal metabolic rate was −36 per cent March 4, 1936, after the patient had been on thyroid extract since February 9, 1936, the basal metabolic rate had increased to −25 per cent. QRS complexes were unchanged, T waves had increased in amplitude, and P R time had decreased to 0 44 second April 8, 1936, after another month on thyroid extract when the basal metabolic rate was 0 per cent, the heart rate was more rapid The amplitude of the QRS complexes and T waves had increased and were of good amplitude. The P-R time had decreased further and was now 0 32 second in Lead II

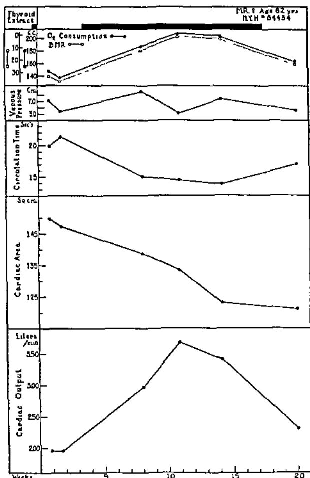


FIG 44

Effects of Thyroid Extract on Oxygen Consumption, Basal Metabolic Rate, Venous Pressure, Circulation Time, Cardiac Area, and Cardiac Output over a Period of Twenty Weeks in a Woman 62 Years of Age, Suffering from Myxedema Before administration of thyroid extract the basal metabolic rate was low, the circulation time prolonged, the heart large, and the cardiac output low With administration of thyroid extract the basal metabolic rate increased, the circulation time became shorter, the heart shadow decreased in size, and the cardiac output increased, until all values were within normal range The last observations were made eighteen days after thyroid extract had been discontinued and show that the basal metabolic rate decreased, the circulation time had increased, and the cardiac output had decreased The heart size had not changed (Stewart, H J, Deitrick, J E, and Crane, N F Studies of the circulation in patients suffering from spontaneous myxedema *J Clin Investigation* 17 237, 1938.)

pressure make it appear unlikely that all of the increase in heart shadow is due to pericardial fluid alone The demonstrated enlargement of many of the heart muscle fibers may add up to some increase in size of the organ.

Prolongation of P-R time and low amplitude of QRS-T complexes (Fig. 43) are other cardiac manifestations which are reversible. The cardiac output per minute and per beat is decreased and the circulation time is slowed, roughly in inverse

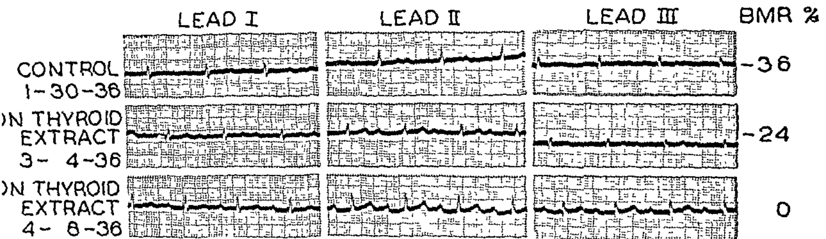


FIG. 43

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and less puffy. The body temperature rises. Anemia disappears if it has been present. As these changes go on, the basal metabolic rate rises, serum cholesterol decreases, the heart becomes smaller, the cardiac output increases, the circulation time becomes shorter, the P-R time decreases, and the amplitude of the QRS-T complexes increases (Fig. 43). Normal values may be attained for these objective measurements.

Complications

Angina Pectoris

If angina occurs while the patient is receiving thyroid extract, the drug should be discontinued, and the basal metabolic rate measured. It may then require careful manipulation of the dosage so that the basal metabolic rate remains below the level of induction of angina, and yet high enough for the patient to be free of as many symptoms of myxedema as possible Myxedematous patients who have angina may not tolerate even small doses of thyroid extract without exacerbation of their symptoms

Coronary Thrombosis

Thyroid extract is discontinued if coronary thrombosis occurs Treatment is the same as for any other patient who suffers this accident. When heart failure occurs it too is treated by the customary measures.

Patients with myxedema who are receiving ration doses of thyroid extract should be kept under careful supervision at regular intervals even after the dosage has been regulated.

SUMMARY

Thyroid extract in myxedema brings about dramatic improvement Pudgy, sluggish, mentally retarded individuals who have obvious stigmata of myxedema are converted into normal appearing and normal reacting ones by replacement therapy with this substance.

The most common cardiac complications of hypothyroidism are angina pectoris, coronary thrombosis, and heart failure. When *angina occurs* attempts are made to manipulate the dosage of thyroid extract so that the highest basal metabolic rate that is possible without the occurrence of this *symptom* is maintained. Should coronary thrombosis be a complication thyroid extract is discontinued until the patient recovers Whether the drug can be given again and in what amounts depend on the functional capacity of the heart after the myocardial infarction has healed as well as on the existence of *residual angina*.

proportion to the basal metabolic rate (Fig. 44). These increase when the basal metabolic rate rises with the administration of thyroid extract.

In addition to the signs and symptoms of myxedema these patients may have evidence of congestive heart failure. Moreover myxedematous patients may suffer from attacks of angina and have myocardial infarctions. Whether the incidence of these is out of proportion to the number of cases to be expected for the age group cannot be stated. These patients also exhibit anemia, which increases the load on the heart.

TREATMENT

Thyroid Extract Regimen

The treatment of myxedema consists in replacement of the thyroid hormone which the gland fails to secrete with thyroid extract, and restoration of the basal metabolic rate to a normal level. This is of special interest in treatment of the cardiac condition, for if the basal metabolic rate is raised too rapidly myxedema patients may suffer attacks of angina and of coronary thrombosis. Consequently thyroid extract is given cautiously in small doses and its administration is best carried out while the patient is under observation in the hospital. The dosage is 0.015 Gm daily for a week to ten days, increasing to 0.03 Gm. for one week to ten days, then to 0.06 Gm. for a week to ten days, then to 0.12 Gm., 0.18 Gm, and 0.24 Gm if necessary, with a week to ten days on each successively higher dose. The basal metabolic rate and the cholesterol level should be checked before each increment of the thyroid extract, and the dose is increased until the basal metabolic rate has approached normal. Subjective and objective changes may be apparent in a week after beginning therapy. If adverse symptoms appear, the drug is discontinued for a few days. It may be found that the highest dosage without symptoms is as far as the drug can be pushed After attaining the optimal level of the basal metabolic rate it may require some manipulation of the dosage in order to maintain it—perhaps 0.12 to 0.18 Gm daily. Many physicians skilled in the care of thyroid disease are of the opinion that, with the patient under observation in the hospital, larger amounts of the drug may be given than those listed, and the progress hastened. The initial doses may be 0.06 Gm daily if this course is followed If there is marked anemia, iron may be given

Course Under Treatment

The schedule outlined above demands extreme caution If there are cardiac symptoms patients should be given thyroid extract when they are at rest in bed, either in a hospital or at home Many patients with hypothyroidism who have no complications may remain ambulatory so that admission to the hospital is not necessary. Larger amounts of thyroid extract can frequently be used at the beginning and the increments added more rapidly. When the ambulatory schedule is used the patients should be seen by the physician at frequent intervals to detect untoward response and cardiac complications should they arise.

Under treatment the patient gradually becomes more alert and energetic. His heart rate increases and his face becomes more expressive. The skin becomes warmer

CHAPTER 16

Pulmonary Heart Disease

(Chronic and Acute Cor Pulmonale)

DEFINITION

The term pulmonary heart disease is used to refer to those instances in which cardiac embarrassment results from lesions primarily localized in the lungs. Congestive heart failure may be caused by the increased load on the heart Dyspnea and cyanosis may be prominent manifestations in some cases because of the interference with gas exchange in the lungs. Pulmonary hypertension may be present.

CHRONIC COR PULMONALE

Pathologic Physiology

Richards and his associates reported the effects of digitalis in chronic cor pulmonale They studied patients with chronic cor pulmonale in cardiac failure as well as patients who had recently been in cardiac failure but were compensated at the time of observation The patients had chronic pulmonary disease, evidence of right heart enlargement or failure, marked cyanosis, but no other demonstrable etiology of their heart disease Chronic pulmonary heart disease in this study was occasioned by the following pulmonary lesions· bronchial asthma, chronic bronchitis, and pulmonary emphysema in one case, bronchial asthma and chronic pulmonary emphysema in another; chronic bronchitis, bronchiectasis, pulmonary fibrosis, and chronic pulmonary emphysema in another, chronic pulmonary tuberculosis, hydropneumothorax, multiple small pulmonary emboli, and pulmonary emphysema in another, silicosis and chronic pulmonary emphysema in still another. These cases are cited as combinations of pulmonary diseases which can give rise to chronic cor pulmonale clinically.

The cardiac output may be greatly increased or may be normal. Other physio-

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The avoidance of respiratory infections and their prompt treatment with antimicrobial agents may prevent acute heart failure

When *heart failure* occurs the use of some or all the measures employed in the treatment of the more common forms of decompensation are employed· one of the preparations of digitalis, aminophyllin intravenously or by rectum, one of the mercurial diuretics, oxygen, low salt diet, restriction of fluid intake, and rest in bed are most frequently required. For some patients with chronic cor pulmonale exhibiting polycythemia and a high hematocrit level, occasional moderate venesection has recently been advocated.

The common causes of chronic cor pulmonale and their treatment are as follows

Pulmonary Fibrosis

The parenchymal tissue of the lungs shows diffuse fibrotic changes. Areas of emphysema—even to the extent of formation of bullae—may be interspersed in areas of fibrosis Chronic and acute forms of the disease occur. With the acute form and with progression of the chronic form the heart fails Cyanosis and dyspnea are pronounced In the chronic forms the pulmonary markings are accentuated and extend to the periphery of the lungs in roentgenograms

Treatment. When seen before the onset of congestive heart failure, patients should be advised to remain within their functional capacities Respiratory infections should be avoided A dry moderate climate near sea level may be found to afford the most comfort. There is no known therapy for the fibrosis. When heart failure appears it is treated by the usual measures rest in bed, digitalis, and mercurial diuretic drugs Digitalis may not be so beneficial as it is in other forms of heart failure The use of oxygen may afford relief when there are exacerbations of symptoms

Pulmonary Arteriosclerosis

Pulmonary endarteritis obliterans (Ayerza's disease) is due to sclerotic changes in the pulmonary arteries or arterioles, resulting in narrowing or obliteration of their lumens Cyanosis is so extreme in Ayerza's disease that these patients are known as "black cardiacs" The prominent components of the sydrome are marked pulmonary hypertension, severe dyspnea, marked cyanosis, and weakness. The vessel markings in roentgenograms may be prominent and appear cordlike and simulate small branches Congestive heart failure may result

TREATMENT There are no measures which alter the progress of the disease. Respiratory infections and high altitudes should be avoided Heart failure usually ensues and is treated with the usual measures, temporary benefit may be derived from oxygen therapy The progress of the disease is often very rapid.

Asthma and Bronchitis

Repeated attacks of asthma and of bronchitis over a period of many years put a burden on the heart and result in hypertrophy of the right side of the heart *Asthma and bronchitis may result in emphysema.* Heart failure may occur after many years

logic findings which may be present to a greater or lesser degree are anoxia, polycythemia, hypervolemia, and pulmonary hypertension. The alteration in pulmonary function may lead to anoxia The anoxia may cause the increase in cardiac output, and it may be the factor which initiates polycythemia and hypervolemia. The high cardiac output is maintained as long as the *optimal diastolic stretch* of the muscle fibers is not exceeded (Starling's Law of the Heart, pp 2, 69). If this occurs the cardiac output decreases and heart failure is precipitated. However, even in failing the cardiac output remains higher than normal.

Effect of Digitalis

With the exhibition of digitalis in the form of digoxin 1.0 to 1.5 mg. intravenously—in the observations reported by Richards and his associates—the cardiac output increases again within one-half to two hours, just as it increases in patients with ordinary forms of heart failure. As compensation is restored by the continued use of digoxin and other therapies the cardiac output declines toward normal, the *pulmonary artery pressure decreases almost to normal, the blood volume and* hematocrit levels fall toward normal, and the arterial oxygen saturation of the blood rises The cardiac size decreases. Cyanosis and dyspnea decrease.

It appears therefore that digitalis exerts the same effect in chronic cor pulmonale with heart failure, which may assume the form of high cardiac output failure, that it does in the more common forms of heart failure of the low cardiac output form—it increases the cardiac output and results in a decrease in the cardiac size.

Pulmonary fibrosis, pulmonary arteriosclerosis, chronic emphysema, chronic asthma and bronchitis, and silicosis have the same effects on the heart and circulation, but of course varying in degree: cyanosis and dyspnea, accentuation of P_2; predominant strain on the right side of the heart; right ventricular enlargement, and *prominence of the pulmonary artery in roentgenograms, right ventricular* hypertrophy and increased amplitude of P waves in electrocardiograms, increase in red blood cell count and in hemoglobin; and decrease in vital capacity.

Treatment

General Principles

The prolonged use of *oxygen* should be avoided as it may lead to alkalosis or carbon dioxide narcosis. When the latter occurs patients become drowsy, then confused and disoriented, and finally stuporous They recover after oxygen is reduced. Oxygen may be used intermittently or in lower concentrations at first with a gradual rise to 50 per cent. In severe cases it may be best to give the oxygen under positive pressure, either expiratory or continuous It may be required for emergency use and over varying lengths of time.

Sedatives are to be used with care These patients are especially sensitive to morphine, which decreases respiration and stops the cough reflex

The use of *one-sixth* molar sodium lactate and other *alkalies* may cause alkalosis.

The use of a *bronchodilator* such as vaponephrin as an inhalant several times a day may be of benefit when there is obstructive emphysema. The vasodilator may be vaporized from a pressure tank of air or of oxygen. Afterwards patients should be encouraged to *cough and raise sputum*. In severe cases suction may be used.

Pulmonary Emboli

Chronic cor pulmonale may also follow repeated showers of small emboli or one or more large emboli In the beginning there may be acute cor pulmonale. Embolectomy, if carried out promptly, may be life-saving, but this procedure carries a high mortality. If the patient survives the acute episode anticoagulant therapy should be used. If the patient recovers, the areas of pulmonary infarction are replaced by fibrous tissue which may result in chronic cor pulmonale. The usual measures are employed when heart failure occurs

Other Causes of Chronic Cor Pulmonale

Amyloid disease of the lungs (p. 356) may be the cause of chronic cor pulmonale. Sickle cell anemia (p. 357) may produce syndrome of chronic cor pulmonale, this probably results from frequently repeated changes in the pulmonary circulation when the crises occur.

ACUTE COR PULMONALE

Acute cor pulmonale results when acute increase in the pressure in the pulmonary circuit occurs. There are two common causes: (1) overloading the circulation with fluids, most commonly by the intravenous route, and (2) pulmonary infarction due to pulmonary emboli

Overloading the Circulation with Fluids

Frank pulmonary edema may result from overdistention of the vascular tree with fluids This can usually be avoided by detecting the onset of or increase in dyspnea and cyanosis, and the appearance of venous distention and of râles at the lung bases Patients may complain of tightness in the chest Accentuation of P_2 appears or increases The electrocardiographic changes are similar to those described in pulmonary infarction (p. 348), the appearance of S_1 being especially noteworthy.

Treatment

Prompt therapy may be life-saving. When the symptoms and signs of acute cor pulmonale appear, the infusion should be discontinued if possible. If continued administration appears necessary the fluid should be given subcutaneously or at a greatly reduced rate. Aminophyllin may be given intravenously Oxygen may be required Rapid digitalization as well as the other measures used in treating acute heart failure may be indicated.

Pulmonary Infarction

The occurrence of pulmonary infarction should be kept in mind in patients in the postoperative period and in those suffering from thrombophlebitis. Detection of this condition may be difficult· patients may complain of precordial distress or tightness in the chest which may be confused with the pain occurring in myocardial infarction The blood pressure falls and the clinical features are those of

TREATMENT. Attacks of asthma and of bronchitis should have appropriate treatment when they occur. Recently ACTH has been found to provide relief from prolonged attacks of asthma. Acute bronchitis is frequently overlooked, or may be thought to be bronchopneumonia because of fever and the presence of diffuse râles in the chest. When it occurs in patients with heart disease it may precipitate heart failure. Patients should remain in bed and should avoid chilling and changes in temperature. Steam inhalations with tincture of benzoin every three to four hours for fifteen to twenty minutes may give relief. Chilling should be avoided when sweating follows the steam inhalations. It is best not to cool the room at night by opening the windows. Oxygen may be beneficial. It will of course be necessary to stop oxygen during the steam inhalations. Aminophyllin 0.24 to 0.48 Gm. intravenously or by rectal suppository in 0.5-Gm. amounts may be of benefit. Penicillin may be used in case the bronchitis results from organisms which are sensitive to it. When heart failure occurs it is treated in the usual manner, digitalis and mercurial diuretics being commonly employed. A bronchodilator such as vaponephrin inhalation three to four times a day may be beneficial.

Emphysema

In pulmonary emphysema the alveoli are distended and the lungs are voluminous. The chest is barrel-shaped, there is difficulty in getting air in and out of the lungs, expirations being extremely prolonged. In the x-ray of the chest the lungs show decreased density indicating hyperaeration. There may be bullae of varying size.

TREATMENT. An abdominal binder may afford relief from dyspnea by elevating the diaphragm. Pneumoperitoneum, used in a few patients with diffuse obstructive emphysema, is said to have resulted in increased ability to raise sputum and in lessening of dyspnea. When heart failure occurs the usual measures are used. It may be necessary to use oxygen. Oxygen and helium may be more effective than oxygen and air, because helium is lighter than nitrogen. Inhalations of vaponephrin, a bronchodilator, three to four times a day may be beneficial. With restoration of compensation by the use of digitalis, mercurial diuretics, and other measures the augumented cardiac output decreases, and the heart becomes smaller, the blood volume and hematocrit fall, and the oxygen saturation of the arterial blood rises. A few attempts have been made in patients with advanced emphysema to enlarge the thorax and ease the depression of the diaphragm by removal of several costal cartilages on each side from their sternal attachments. Use of one-sixth molar sodium lactate and alkalies in these patients may cause alkalosis. They may be sensitive to morphine.

Pneumoconiosis—Silicosis and Asbestosis

Silicosis and asbestosis result from inhalation of these dusts giving rise to chronic changes in the lung tissue. Areas of fibrosis interspersed with areas of emphysema give a "snowstorm" appearance in the x-ray of the chest. The secondary changes are similar to those in other pulmonary lesions. The cardiac stress may result in heart failure, which is treated in the usual manner.

PULMONOCARDIAC FAILURE

Included in the group of patients suffering from pulmonocardiac failure are those who have deformities of the thorax and spine which finally result in decrease in the functional capacity of the lungs and cardiac embarrassment either by compression or by torsion of the heart and the great vessels. There may be kyphosis, scoliosis, lordosis, or combinations of these Patients with right-sided dorsal kyphoscoliosis in particular suffer habitual dyspnea which may severely limit activity. Other patients exhibit marked depression of the sternum: the so called funnel chest or pectus excavatum. This deformity may compress the heart and thereby embarrass the organ or it may compress large vessels in the mediastinum. When compression of the arteries occurs decrease in volume—or even complete absence—of pulses in the arms may be observed There may be numbness and tingling of the arms and hands. When the brachial arteries are compressed patients use the scaleni and shoulder muscles to hunch the shoulders to relieve the obstruction and permit circulation to the arms

The signs and symptoms in pulmonocardiac failure are due partly to the changes in the heart and partly to the restriction of the available pulmonary space The common symptoms are palpitation, attacks of syncope, and aggravation of dyspnea by exertion or change in position. The vital capacity is reduced to one half or less. The ratio of residual air to vital capacity is doubled Consequently the respiratory volume increases but less oxygen is removed from the inspired air. The carbon dioxide content of the arterial blood may be high The electrocardiograms may be difficult to evaluate in these patients since the axis deviation is altered by rotation Location of the chambers may require angiocardiography These patients are subject to pulmonary infections; especially bronchiectasis together with pulmonary emphysema

The distortion of the chest occurs over a number of years, accordingly the heart and great vessels undergo some accommodation and may follow the natural state of growth, so that the heart may not be large. In other instances there is right ventricular hypertrophy which points to increased work and to increased pressure within the pulmonary circuit The cardiac output may be increased, this may be due in part to the chronic anoxia. Heart failure in these patients is of the so-called high output form

These patients may get on well for long periods but gradually the deformity progresses, dyspnea increases, pulmonary infections occur, and pulmonocardiac failure overtakes them The average age at death is 30 years Pulmonocardiac failure with congestion and edema may come on rapidly and be fatal The cause of fainting in these patients is not known.

Treatment

The early use of proper braces and supports may retard the progress of the chest deformity. Breathing exercises and attention to posture may help. For other patients spinal fusion operations to hold the spine in place may be indicated Patients with marked chest deformity with habitual dyspnea should not travel by air. Heart

shock. There may be cyanosis and dyspnea. The appearance of appropriate signs in the chest may make the diagnosis apparent. P_2 is accentuated. A series of electrocardiographic changes may occur which in certain instances are typical of pulmonary infarction and may be diagnostic. On other occasions the configuration of the electrocardiogram may be confused with that resulting from myocardial infarction The electrocardiographic alterations associated with pulmonary infarction are more rapid than is usually the case in coronary thrombosis. Transient bundle branch block may appear. Roentgenograms of the chest may show a typical wedge shape of increased density in the pulmonary field, or a platelike shadow. Acute heart failure may ensue.

Treatment

The source of the emboli should be discovered if possible. One will have to decide upon tying off peripheral veins if these are implicated, upon embolectomy, and upon the use of anticoagulants (Chapter 4). Acute heart failure is treated in the usual fashion· intravenous aminophyllin is given slowly; rapid digitalization may be indicated, the use of oxygen may be essential When digitalis is given the configuration of the T waves and RS-T segments may be altered in such a way that the pattern expected in acute cor pulmonale does not appear, digitalis, however, does not alter the S wave changes

INTERSTITIAL EMPHYSEMA

Interstitial emphysema may give rise to symptoms which may be confused with myocardial infarction Air accumulates in the anterior mediastinum in the tissues between the sternum and the heart Characteristically, with each heart beat, "crunching" of air in the loose tissue occurs and causes a noise which may be heard by the patient. Frequently the noise can be heard before the stethoscope is applied to the sternal region. Interstitial emphysema is characterized usually by the sudden onset of substernal pain in young individuals and by detection of the crunching sound Fever, leukocytosis, fall in blood pressure, and increase in sedimentation rate, which characterize myocardial infarction, may not be recorded Formerly it was thought that electrocardiographic changes did not occur More recently moderate alterations in the electrocardiographic pattern have been recorded The diagnosis is confirmed in lateral roentgenograms of the patient's chest in which free air is demonstrated under the sternum. If large amounts of air escape from the alveoli, a small pneumothorax with air at the apices may be detected.

Treatment

The patient should remain quietly at rest in bed until it is certain that further increase in free air is not likely, until the symptoms subside, until the crunch disappears, and until the nature of the whole episode is clear Patients should avoid sudden exertions for some time afterward. I have not seen pneumothorax occur in such degree that removal of the air was required.

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failure receives the usual treatment. I have observed patients who required long periods of residence in oxygen tents in order to facilitate even moderate restoration of compensation, but this should be avoided if possible because it leads to alkalosis. Other patients exhibit abnormal rhythms, such as auricular paroxysmal tachycardia, which resist therapy. Care must be exercised in the use of sedatives in these patients, who are especially sensitive to morphine.

On recovery from failure activity should be limited. Maintenance of the medical regimen may delay the recurrence of failure Freedom from respiratory infections and prompt treatment with antimicrobial agents may prevent attacks of failure. Steam inhalations and oxygen may be required.

Surgical means have been used to reconstruct the chests of young patients with the funnel deformity. The attachment of the ribs to the sternum is freed; the sternum is brought forward and anchored by realignment and reattachment of the ribs to new locations on the sternal margin. This operation should be carried out in late childhood and in young adults before embarrassment of the heart has become marked and before irrevocable damage to the cardiac and pulmonary systems has resulted. There have been a few reports of success after such procedures.

Section of the scaleni on both sides has afforded relief from the numbness and tingling in the upper extremities when the brachial arteries are compressed

Pregnancy in patients with chest deformities is discussed in Chapter 28.

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rate. The Q-T time may be prolonged. The electrocardiographic alterations are not specific. Smith and Furth as well as Dock have described a number of patients—suffering from possible variants of beriberi heart disease—who have exhibited heart failure, large hearts, mural thrombi with tendency to pulmonary emboli, and bundle branch block.

DIAGNOSIS

The diagnosis cannot be made accurately in retrospect It should be established before specific treatment is started. It is not unusual to see patients begin to improve with the institution of the hospital diet When other measures for treating heart failure are started improvement begins promptly. The crucial test of improvement on vitamin B complex alone is rarely carried out

TREATMENT

Vitamin B_1

The patient should be kept at rest in bed. If he is not so sick that all available measures are urgently required at once, he might be kept on his usual diet with the addition of only vitamin B_1. If this cannot be done, the hospital diet plus the vitamin B components may be tried before diuretics are given Crystalline vitamin B_1 (thiamine hydrochloride) may be given intravenously, intramuscularly, or orally. If absorption from the gastrointestinal tract is retarded or the patient is very sick, the intravenous route should be chosen Thirty to fifty milligrams are given twice a day. Five to ten milligrams twice a day may be adequate in mild cases Brewers' yeast or wheat germ, given in large amounts, can be used on cereals or in cold milk, eggnogs, and chocolate drinks A high caloric diet rich in vitamin B foods is indicated Whole grain bread, cereals, lean pork, steak, kidneys, liver, heart, vegetables cooked without soda, and milk should be included

With the institution of these measures in optimal cases, diuresis occurs and the patient becomes free of edema and serous effusions, the cardiac rate slows, the heart becomes smaller, the venous pressure falls, the circulation time lengthens, peripheral vasodilatation is corrected, and compensation is restored.

Other Measures

Other adjuvants may be required for very sick patients if it seems unwise to await the gradual beneficial effects of the vitamin B products. The fluid intake is restricted and a low salt diet given. However, it may not be possible to keep the salt intake under 5.0 Gm because of the high protein intake which is required. Ammonium chloride may be necessary in addition to the mercurial diuretics. I prefer to wait for the effect of the foregoing measures to become apparent before using digitalis In fact, I use this drug only if the other measures do not provide rapid diuresis and improvement, because fragmentation of cardiac muscle fibers with hyaline and fatty degeneration has been reported in beriberi heart disease.

Occasionally, patients who appear to be suffering from beriberi heart disease or from some features of the syndrome are not benefited by vitamin B_1 alone or with

CHAPTER 17

Beriberi Heart Disease

ETIOLOGY

Beriberi heart disease results from (1) prolonged deprivation of vitamin B_1; (2) chronic conditions (such as prolonged infections, hyperthyroidism, or alcoholism) which consume more vitamin B than is available in the usual diet, and (3) faulty absorption of vitamin B components of the diet, especially the B_1 factor, owing to chronic gastrointestinal disease In oriental countries the disease is a consequence of inadequate food intake In most of the cases of this disease seen in the United States, however, high intakes of alcohol together with inadequate diet are the precipitating factors. Beriberi heart disease is a so-called "wet" manifestation of vitamin B deficiency.

PATHOLOGIC PHYSIOLOGY

The pathologic physiology of the circulation in beriberi heart disease resembles that of ordinary heart failure in that the venous pressure is elevated, but it differs from congestive heart failure in two important respects:

1. The circulation time is short in beriberi heart disease, whereas in congestive heart failure it is prolonged.
2. The cardiac output is increased in beriberi heart disease, but is low in the usual forms of congestive heart failure.

It represents one variety of so-called high output cardiac failure Signs of peripheral neuritis may be detected. Anemia may be present.

CLINICAL MANIFESTATIONS

The clinical picture may be one of congestive heart failure with edema, ascites, venous engorgement, but with peripheral vasodilatation The heart is enlarged. The electrocardiogram may show low amplitude of the QRS-T complexes with a rapid

CHAPTER 18

Diseases Which May Have Cardiac Manifestations or Simulate Cardiac Disease

In this chapter a number of unrelated diseases will be discussed. For the most part they form a small segment of cardiovascular disease, although certain of them, such as periarteritis nodosa and disseminated lupus erythematosus, are encountered with increasing frequency. In certain of these the cardiac manifestations form sometimes a small, at other times a large component of the clinical picture For example, the clinical manifestation of periarteritis nodosa may in large measure pertain to the heart—pericarditis, coronary artery changes, myocardial infarction, and heart failure, all requiring therapy

In the other subjects included in this chapter are diseases or syndromes which may simulate cardiac disease For this reason they are the concern of physicians especially interested in the treatment of diseases of the heart. In this group are the scalenus anticus syndrome, hiatus hernia, and atypical gallbladder disease in which symptoms may be like those in angina pectoris The early picture of dissecting aneurysm of the aorta may be difficult to differentiate from myocardial infarction and the management rightly belongs in this chapter.

ACROMEGALY

Pathology

Marked changes in the cardiovascular system are a characteristic late development in acromegaly. In most patients who succumb to this disease, heart failure is the cause of death The cardiac size is beyond that expected not only for the build and muscular development of the patient, but also for the splanchnomegaly. The walls and the lumens of the blood vessels are enlarged. Hypertension, valvular disease, arteriosclerosis (an almost constant finding), and elevation of basal

the usual measures for treating heart failure. Perhaps after a certain period of deprivation of vitamin B_1 irreversible changes in heart muscle will occur, at which point in the natural history of the disease heart failure in the usual sense prevails Accordingly there may be in the later stages not only features of beriberi heart disease but also components of congestive heart failure in the usual sense.

After-treatment

After recovery the patient should remain on a diet high in vitamin B and avoid the use of alcohol The patient should be instructed to continue with the hospital diet. It must be impressed upon him that he is unable to manufacture or store vitamin B_1, and that he maintain a continued intake of the vitamin to avoid recurrence of the disease.

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The rhythm is usually normal, but auricular fibrillation has been recorded. Left axis deviation is more common than right. Primary systemic amyloidosis may simulate chronic constrictive pericarditis. The combination of elevated venous pressure, low pulse pressure, small cardiac movements, low electrocardiographic voltage, hepatomegaly, low serum albumin with normal globulin, albuminuria, dependent edema, and ascites may cause confusion with Pick's disease.

Heart failure is treated by the usual measures.

THE ANEMIAS

Hypochromic Anemia

Patients with *hypochromic anemia* as well as patients with *pernicious anemia* may exhibit cardiovascular manifestations With the low red blood cell count and hemoglobin the circulation is speeded up, the cardiac output is increased, and the circulation time shortened in order to maintain the oxygen requirements of the tissues. Due to the load that this accelerated circulation puts on the heart, these patients may develop typical congestive heart failure with a high cardiac output, so-called *high output failure* Breathlessness and increased heart rate are accompaniments of the anemia. All of the foregoing signs may be aggravated by the tendency to fluid accumulation due to the low level of serum proteins.

Treatment

If the signs and symptoms are not marked they may be dissipated with the restoration of the red blood cell count and hemoglobin by iron or liver therapy It may be advisable, even necessary, to treat the heart failure by the same regimen as is used in other patients with heart failure low salt, high protein diet, limitation of fluids, and use of mercurial diuretics and ammonium chloride The factor of heart failure should be clearly established before using digitalis, otherwise this drug may make the patient worse. It is obvious that unless the heart has become greatly dilated in the course of failing, benefit could not be expected from its use If the venous pressure is elevated, restoration of some degree of compensation should be attained before blood is given intravenously, too rapid an increase in the blood volume may increase the load on the heart. If additional blood is urgently required, however, it can be provided as small, repeated transfusions given slowly. This procedure may correct the depletion of red blood cells and hemoglobin more quickly than the exhibition of iron or liver therapy.

Sickle Cell Anemia

The manifestations of sickle cell anemia may mimic those of rheumatic heart disease because of the concurrent joint manifestations and the overactivity of the heart accompanied by cardiac enlargement with a configuration which suggests that seen in mitral stenosis The murmur may be due in part to overactivity and in part to change in viscosity of the blood. The enlargement of the heart with prominence in the pulmonary artery region may result from cor pulmonale. There may be thrombotic occlusions of small and medium-sized arteries of the lungs, with

metabolic rate are apparently not the cause of enlargement of the heart. Hypertrophy of muscle fibers is not a constant finding even in the largest hearts. Diabetes, which may also be present, may contribute to changes in the coronary arteries.

Clinical Manifestations

The patients complain first of weakness and fatigability which is out of proportion to their muscular development, and of palpitation and dyspnea on exertion Attacks of syncope soon occur and the patient becomes incapacitated. As the disease progresses pallor appears, asthenia increases, breathlessness is constant, the pulse becomes rapid and irregular, and the patient usually succumbs to heart failure. Electrocardiographic changes are neither constant nor specific. There may be left axis deviation, late in the disease there may be splitting and widening of the QRS complexes as evidence of myocardial damage, there may be T wave deformities and abnormalities of rhythm

In Courville and Mason's series the average age of patients exhibiting heart failure was 48 years; the average age of those dying of heart failure was also 48 years.

In the late stages the manifestations of heart failure do not differ from those in other types of cardiac decompensation The rapid pulse may not respond to digitalis. Cyanosis becomes marked. Edema, pulmonary congestion, and Cheyne-Stokes respirations appear.

Treatment

Neither heart failure nor other evidences of cardiac pathology require treatment other than the usual measures.

AMYLOIDOSIS

Pathology

Amyloid disease may involve the heart and lead to heart failure. This involvement is more common in primary systemic amyloid disease than in the secondary form, which is the result of a chronic suppurative disease. It is the systemic manifestations that afford a clue to amyloid disease as a cause of cardiac failure. The factors responsible for failure may, however, be difficult to evaluate since amyloid disease may involve the lungs causing chronic cor pulmonale. Anemia, coronary arteriosclerosis, and hypertension may all be present. Amyloid may be diffusely scattered through the myocardium or it may have a nodular distribution Both the auricular and the ventricular musculature show lesions and, less frequently, the pericardium. Amyloid deposits may appear in all layers of the blood vessels in the myocardium, and there may be valvular endocardial deposition of amyloid. Biopsy of apparent lesions which are accessible and the Congo red test may lead to the correct diagnosis.

Clinical Manifestations

The course of the disease may be slow or rapid, and in the primary types does not show regression. In the electrocardiogram there may be low amplitude of the QRS complexes, prolongation of the P-R conduction time, and 2:1 heart block.

more difficult to treat because of the great number of communications and the tendency to recur. Certain of the congenital fistulas may be difficult to differentiate from hemangiomas.

Clinical Manifestations

The typical physical signs of an arteriovenous fistula are thrill and bruit. These vary in intensity with the number and size of the communications. When the fistulas are sufficiently large certain compensatory changes take place in the cardiovascular systems: The blood volume and the cardiac output, size, and rate increase. The systolic pressure rises and the diastolic falls. These may lead to dyspnea and later to *congestive heart failure*, a cause of decompensation which must not be overlooked. If a limb is involved its volume will increase. Because of the increased local circulation the temperature may be higher than that of a corresponding area of the body which is not involved. When the fistula opening can be obliterated by pressure there is prompt slowing of the heart rate, and fall in systolic and rise in diastolic pressure. Visualization of the communication or communications with the extent of the aneurysmal dilatations may be achieved by radio-opaque injections into the affected artery

Arteriovenous Fistulas of Lung

Arteriovenous fistulas of the lung are being described and recognized with increasing frequency The lesions are also known as *arteriovenous varix* or *aneurysm, angioma*, and *cavernous hemangioma*. They are of congenital and often familial origin. There may be associated vascular lesions of the skin, mucous membranes, and lip, and thereby be of the general nature of hereditary hemorrhagic telangiectasia. These fistulas are composed of a distended, thin-walled afferent artery, distended efferent veins, and an intervening loculated sac or labyrinth of distended vessels. The vessels become dilated, and more communications form and predispose to rupture with pulmonary hemorrhage or hemothorax The lesions are multiple in approximately half of the cases. They are more frequent in males, and are more commonly discovered in young children or young adults. Fluoroscopic examination shows a lobulated opacity which may pulsate; there may be hilar pulsations Angiocardiograms are useful in diagnosis.

The circulatory derangement is dependent upon the amount of unoxygenated blood shunted into the pulmonary veins. When the shunt is large enough cyanosis and clubbing appear. There may be dyspnea on exertion, hemoptysis, attacks of dizziness and unconsciousness, cerebral vascular accidents, and other symptoms associated with polycythemia A murmur may be heard over the lesion. There is increase in the red blood cell count, hemoglobin, and hematocrit. The blood volume increases The cardiac output remains normal or may be increased in large shunts, and the blood pressure may be normal. The heart may be of normal size. *Heart failure is uncommon.*

Treatment

Acquired Arteriovenous Aneurysms

These defects are more easily repaired by surgical means than are the congenital variety. If the site of the communication can be found, the aneurysms may be

organization and canalization of the occasional discrete thrombi. Heart failure may be precipitated by a bout of fresh thromboses. On the other hand thromboses may not be present, but there may be thickening of the walls of the small and medium-sized arteries and arterioles of the lungs with reduction in caliber of their lumens. These patients have too little hemoglobin to show the cyanosis of Ayerza's disease.

The sickling trait is present in 7 to 10 per cent of the Negro population in the United States. Clinical sickle cell disease appears in 2 to 4 per cent of these. It is estimated that there are approximately 135,000 sufferers of the disease in the United States. The trait is transmitted as a true mendelian dominant characteristic.

The disease is characterized by crises in which large numbers of sickle cells appear, which move sluggishly in capillaries, causing thromboses. The disease is accompanied by chronic hemolytic anemia, the acute exacerbations are characterized by severe joint, muscle, and abdominal pains; fever; and massive hemolysis with jaundice. The pains are due to local thromboses; the jaundice is attributed to resolution of the thrombi and disintegration of the sickled cells. Characteristic bone changes are demonstrated in x-ray photographs, and there may be leg ulcers.

Treatment

When heart failure occurs due to myocardial changes or to cor pulmonale it is treated in the usual manner Attempts have been made to use anticoagulant therapy during the crises, but dicumarol and heparin have neither prevented nor decreased the severity of crises. Blood transfusions are given as they may be required, care must be exercised if cardiac manifestations are prominent.

Chronic Hookworm Anemia

The cardiac hypertrophy characteristic of this form of anemia is only partially reversible following treatment. As a compensatory mechanism the vital capacity of the lungs increases. The circulation time in these patients is not shortened. Non-specific changes in the T waves of the electrocardiogram may be recorded

Recovery from hookworm infection and reduction in the size of heart are achieved by the use of anthelmintics The hemoglobin increases following the use of iron, liver extract, and high protein diet

ARTERIOVENOUS FISTULAS

Types

There are two types of arteriovenous communications traumatic or acquired, and congenital The *acquired* are much more easily cured than are the congenital. An acquired arteriovenous fistula occurs when there has been trauma to an artery and a contiguous vein. The common causes are gunshot wounds and stabbings, but disease of an artery may result in its rupture into a vein For example, an aneurysm of the ascending aorta may rupture into the superior vena cava, or one of the descending aorta into a pulmonary vessel. Following the arteriovenous communication the enlargement of the vessels becomes aneurysmal. The venous enlargement is greater than the arterial. In the *congenital* type, embryonic vascular tissue grows out in buds and establishes communications between arteries and veins. These are

more difficult to treat because of the great number of communications and the tendency to recur. Certain of the congenital fistulas may be difficult to differentiate from hemangiomas.

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ligated, restoring the continuity of the two vessels. With re-establishment of the circulation in artery and vein both the immediate and associated symptoms and signs disappear. Compensation is restored, the blood volume decreases, the cardiac output declines, and the heart size decreases. It has been pointed out by Holman and others that ligation of the main artery leading to the arteriovenous fistula in the peripheral circulation is contraindicated, as it will almost always lead to gangrene of the limb.

An arteriovenous fistula may be the site of localization for subacute streptococcus viridans septicemia with vegetations in the aneurysm. Cure has been reported by Hamman and Rienhoff following excision of the aneurysm. This, however, would require differentiation from subacute bacterial endocarditis.

Congenital Arteriovenous Aneurysms

Careful ligation and section of the many communications are required in the congenital type This is a time-consuming procedure and may have to be done in stages. Apparent cure or temporary relief may be achieved only to have new communications appear within a short time. So many arterial branches may be interrupted that the carrying of nutrition to the part may be interfered with. When this occurs in an extremity, amputation may be required. When extensive and repeated operations on the extremity are required sympathectomy may increase the vasodilatation of the remaining channels.

Heart failure is treated by appropriate measures Relief will be temporary unless the aneurysm is eradicated.

Arteriovenous Fistulas of the Lung

Small fistulas without symptoms and without significant compensatory mechanisms must be watched carefully but it cannot be predicted when hemorrhage may occur. One case has been reported which benefited from simple ligation of the pulmonary artery The treatment of choice is lobectomy or partial resection for solitary lesions, or pneumonectomy if there are multiple fistulas in all lobes of one lung. At times it is not possible to gauge their extent accurately before operation. Cure may be achieved if all the lesions can be eradicated.

CARDIAC ATROPHY

Definition

Atrophy of the heart has been defined as an acquired reduction in the size and mass of this organ It is a difficult diagnosis to make during life, but its presence can be suspected Hellerstein and Santiago-Stevenson have recently brought together data relating to 85 proved cases and reviewed the literature There are two types simple atrophy and brown atrophy.

Predisposition

Simple atrophy predominates in younger and *brown atrophy* in older subjects, in whom pigment deposition occurs normally with advancing years. The latter is more common and occurs in conjunction with a variety of diseases, most commonly with neoplasms, chronic infection being the next most common factor. The predomi-

nance of neoplasms in the reproductive system of women accounts for the greater incidence of cardiac atrophy in this sex. The predisposing factors are prolonged illness, prolonged bedfastness, and malnutrition when it has progressed to a loss of about one-quarter of the body weight.

The diagnosis of cardiac atrophy in the study referred to was based on decreased weight, increased pigmentation of muscle fibers, atrophy of subepicardial fat, wrinkling of the epicardium, tortuosity of coronary arteries, increase in nuclei-fiber ratio, and decrease in muscle fiber width

Clinical Manifestations

The hearts are small and inactive, with normal or faint heart sounds. Systolic murmurs may be present at the apex; the blood pressure falls with the onset of atrophy, but may remain elevated in hypertensive individuals. In roentgenograms the hearts are small or of normal size. The hearts may be tubular in patients with anorexia nervosa. The electrocardiogram shows lowering of the amplitude of the QRS complexes and T waves and prolongation of the Q-T and of the P-R time, similar to those recorded in experimental starvation The basal metabolic rate is lowered. With all this there is a striking absence of changes in the functional capacity of the heart, since congestive heart failure is rarely encountered It is the impression that in malnutrition the heart participates in the general atrophy of the body, but on the average the heart loses mass to a greater degree than does the body, since the heart-body weight ratio is lower than in normal individuals The low incidence of heart failure is to be attributed to the decreased work of the heart and to the change in myocardial fiber size and capillary fiber ratio Certain of these objective clinical measurements associated with atrophy of the heart are parallel to those recorded in experimental starvation

Treatment

The inference is drawn that the cardiac atrophy is reversible in starvation with recovery such as has been observed experimentally and with inmates in concentration camps Obviously therapy should be directed at restoration of an adequate caloric intake This may be difficult to achieve, for example, in patients with anorexia nervosa and with Simmond's disease

Whether these observations can be turned to clinical use requires exploration. It has already been mentioned in Chapter 11 that resolution of arteriosclerotic lesions is observed at autopsy in patients who have lost weight before death. The fall in blood pressure and decrease in size of the heart in hypertensive patients with loss in weight provide evidence pointing toward a beneficial effect of weight loss in such subjects

CARDIAC HYPERTROPHY OF UNKNOWN ETIOLOGY

In Adults

The literature contains many histories of patients in whom hypertrophy of the heart was the prominent feature, in the absence of any apparent etiologic factors. Accompanying features have been congestive heart failure, abnormalities of rhythm

and of cardiac conduction, mural thrombi, and the distribution of emboli to the lungs and to the systemic circulation. The blood pressure was in some instances low, at any rate it was not elevated. Death either resulted from the gradual progression of heart failure or, in some cases, it came about suddenly. Microscopic examination of the heart after death showed hypertrophy of the muscle fibers In some cases this was the only lesion. In others, there were also varying degrees of fibrosis. Areas of necrosis of old or recent origin were seen. Cellular infiltrations characteristic of acute interstitial myocarditis of the Fiedler type were absent, as were valvular damage and coronary artery changes. In the cardiac cavities thrombi were frequently encountered. The electrocardiographic abnormalities were as follows inversion of the T waves in Lead I or in Leads I and II; low voltage of QRS complexes; premature contractions; auricular fibrillation of paroxysmal or permanent form; paroxysmal auricular flutter; paroxysmal tachycardia arising in the auricles, auriculoventricular system or ventricles, partial and complete auriculoventricular heart block, and bundle branch block.

Clinical Course

The clinical course—if not the microscopic findings—in these patients resembled isolated myocarditis of the Fiedler type. The clinical course also has characteristics similar to those of the cases reported by Smith and Furth, especially the tendency to mural thrombi and embolization with pulmonary infarction. In the association of large hearts and pulmonary infarctions they resemble the cases reported by Dock as a form of beriberi heart disease. Finally there is the group of cases reported by Gouley, McMillan and Bellet as "idiopathic myocardial degeneration associated with pregnancy and especially the puerperium" In them also, mural thrombi and pulmonary and cerebral embolism occurred

Whether there is a relationship between all these types of myocardial lesions having somewhat the same clinical course remains to be seen. It may be that some of them represent different stages of the same process.

Treatment and Prognosis

The main presenting features which require treatment are congestive heart failure, embolic phenomena, and cardiac arrhythmias Heart failure and cardiac irregularities are treated by the customary measures Since anticoagulants may be effective in preventing or postponing mural thrombi or embolic phenomena, heparin or dicumarol may be given a trial. Temporary relief from heart failure may occur, but the course is downhill.

Bernheim's Syndrome

In a recent analysis Evans and White concluded that there is no evidence that Bernheim's syndrome is a true clinical entity. This comprises left ventricular hypertrophy (without right ventricular hypertrophy) of such proportions that the right ventricular cavity is partially occluded by the intrusion of the septum into it. The volume of blood which this chamber can accommodate is assumed to be greatly compromised, leading to the appearance of obstructive signs.

In Children

Cardiac hypertrophy of unknown etiology also occurs in young infants and children. After glycogen storage disease, congenital malformations, and other detectable causes of cardiac enlargement are ruled out, the diagnosis of *idiopathic hypertrophy of the heart* can be made. At autopsy there may be marked endocardial fibrosis which penetrates into the myocardium. The presenting features of these cases relate to congestive heart failure The disease proves fatal within a period of days or months.

DISSECTING ANEURYSM OF THE AORTA

Pathology

Diagnosis of dissecting aneurysm of the aorta is being made correctly with increasing frequency. Whereas in 1934 Shennan's monograph pointed out that the diagnosis was rarely made ante mortem, in recent statistics the correct diagnosis is made in 25 to 50 per cent of the instances, as brought out in the recent survey of Levinson, Edmeads, and Griffith

Dissecting aneurysm is two to three times more common in men than in women, and its incidence is also higher in the Negro race because of the more frequent occurrence of hypertension This lesion occurs most commonly in the ascending aorta and may progress upward or downward. In most instances the tear, which is usually transverse, is in the medial layer, the intimal lesion being secondary. The medial lesion may start as a hemorrhage from a vasovasorum in the media. At other times there is medial degeneration and loss of muscle, elastic, and collagen tissue. In one-half of White's acute cases idiopathic cystic medial necrosis of the Erdheim type was found to be the predisposing lesion. This type of lesion is found in instances of rupture of the aorta in myxedema. Rupture of a normal vessel rarely if ever occurs Rupture through an arteriosclerotic plaque is uncommon It is rarely on a syphilitic basis, is not an uncommon accident in coarctation of the aorta, and occurs in pregnancy Most of the patients have a history of hypertension, although it may occur in normotensive subjects It is most common in the fifth to seventh decades, but occurs in younger people

In dissecting aneurysm separation of the medial layer occurs and rupture through the intima into the lumen forms a communication between the lumen and the medial space. If the adventitious layers can withstand the aortic pressure outward rupture does not occur Blood in the new channel may clot and lead to healing by fibrous tissue. In certain instances the blood channels its way back into the aorta at another point, usually lower down, and a so-called "double barreled aorta" is formed If this occurs, in the course of time the lumen of the dissecting aneurysm is endothelialized and circulation of blood through this channel is maintained Accumulation of blood in the dissecting aneurysm may encroach on neighboring structures or on the lumen of the aorta.

Clinical Manifestations

On rare occasions dissecting aneurysms of the aorta may take place asymptomatically. Commonly, it is accompanied by pain in the chest or in the epigastrium

with radiation to the back. It is sudden and dramatic in onset, and most frequently without relation to effort. It is described as a "tearing sensation." The distribution does not usually resemble that of myocardial infarction. There may be transient syncope

Pulsations in the peripheral vessels may decrease in volume or disappear if the false sac distends and occludes vessels or if the peripheral vessels thrombose due to damage Dissection may extend upward to involve the vessels of the head or downward and involve the renal and iliac vessels. These changes may be transient. After the acute episode an aneurysmal mass may appear on the abdominal aorta and gradually enlarge

Certain *neurologic manifestations* contribute to the diagnosis, paralysis of an arm or the lower extremities with loss of reflexes and sensation, or transient weakness of one or both legs accompanied by numbness and loss of sensation.

Usually the *pulse and respirations increase*. There is rise in temperature. The blood pressure may remain elevated, as a differential diagnostic feature from myocardial infarction, it may fall with shock but not to the level expected in that condition. There may be anemia if much blood is pooled in the dissecting aneurysm There is usually leukocytosis.

Signs of aortic insufficiency appear in a large number of cases. This may be due to tear involving one of the aortic valve commissures, to stretching or dilatation of the aortic ring, or to regurgitation through the intimal tear A *systolic murmur* may appear about the aorta as evidence of compression of its lumen or of the re-entry of blood into the aorta from the dissecting aneurysm

On x-ray examination of the chest a large *supracardiac shadow* may be found. If this increases in size it would be corroborative evidence for dissecting aneurysm In chronic cases angiocardiography may reveal a thickened aortic wall and narrow lumen corresponding to supracardiac shadows or along the course of the aorta if there is replacement of the aneurysm by scar tissue, or a double channel might be demonstrated if the new channel enters the aorta lower down.

When there is damage to a renal vessel there may be *oliguria*, hematuria, and flank pain

Electrocardiographic alterations occur but they are not characteristic. Changes in the T waves and RS-T segments may be in part associated with shock and with anemia. There may be changes similar to those seen in angina pectoris In other instances the pattern may be that of myocardial infarction, which may indeed occur should a coronary vessel be torn and become thrombosed as dissection proceeds, or should a coronary vessel be compressed by the dissecting aneurysm The electrocardiographic pattern may point to acute pericarditis resulting from hemorrhage into the pericardial sac, from uremia, or from myocardial infarction

Consequences

The following end results in dissecting aneurysm of the aorta have been encountered: (1) Rupture into a pulmonary artery; this leads to sudden increases in signs and symptoms of heart failure A large pulmonary artery which pulsates can be seen on fluoroscopy; (2) rupture into the right ventricle; (3) rupture into the pericardium; (4) rupture into the gastrointestinal tract, in which mesenteric vessels may

be torn, with interruption of the blood supply to that tract, (5) tearing of a renal artery; (6) tearing or occlusion of a coronary vessel by outside pressure of the dissecting aneurysm

Differential Diagnosis

Because of the pain the main lesion from which dissecting aneurysm of the aorta requires differential diagnosis is myocardial infarction The occurrence of pain atypical for myocardial infarction; the severity of the pain; the occurrence of transient changes in the pulsations of the peripheral vessels and of neurologic manifestations, the presence of signs of aortic insufficiency, perhaps of sudden onset, in a hypertensive patient with a wide aorta and no serologic signs of syphilis; perhaps maintenance of the blood pressure levels, the absence of typical electrocardiographic patterns of myocardial infarction—all these contribute to the diagnosis of dissecting aneurysm There is reason for making the distinction as soon as possible in order that anticoagulant therapy should not be started

Treatment

The treatment of dissecting aneurysm of the aorta is similar to that for myocardial infarction, with the exception of the use of anticoagulants The patient should be at complete rest As few examinations as possible should be made Sedatives are given as required for pain, which may be difficult to control It may be necessary to provide blood by transfusions should extensive pooling of blood in the aneurysm occur and if shock is more than transient After the acute episode bed rest should be prolonged to allow the fibrous changes in the aneurysm to withstand the increases in aortic pressures associated with activity. Whether wrapping with cellophane will assist these fibrous changes, or surgical replacement by sections of aorta from a blood vessel bank can be accomplished must await further investigation

Prognosis

Death may occur at once or in the first 24 to 48 hours In other instances, patients survive for days or weeks but rupture finally occurs. Other patients survive for months or years In these, blood may re-enter the aorta through a second rupture into its lumen with subsequent endothelization, or less frequently the cavity of the aneurysm is obliterated by the formation of a clot and finally scar tissue Death in such cases results from congestive heart failure, from cerebral accidents, from coronary artery disease, from a second dissection with fatal rupture, or from other incidental diseases

DISSEMINATED LUPUS ERYTHEMATOSUS

Pathology

Lupus erythematosus, one of the diseases more recently designated as collagen diseases, may be associated with cardiac manifestations.

The widespread manifestations of the disease throughout the body facilitate the clinical diagnosis The disease has certain features in common with polyarteritis nodosa, scleroderma, and dermatomyositis, which also belong to the group of col-

lagen diseases. The disease is characterized by involvement of the connective tissue structures of the body and by proliferative and degenerative changes in the collagen structure throughout all the tissues: blood vessels, pericardium, endocardium, myocardium, kidneys, spleen, and lymph nodes. The etiology is unknown The disease may run a fulminating course or be subject to remissions, but is usually fatal.

The disease occurs most commonly in young women in the childbearing age.

Clinical Manifestations

The typical clinical picture is one of prolonged irregular fever, tachycardia, glandular enlargement, and fluid in the joint cavities, together with skin lesions. The patient appears toxic There is increase in sedimentation rate and leukopenia with anemia The platelets may be depressed. The plasma albumin is decreased and the globulin fraction may be greatly increased. There may be involvement of all of the serous cavities with rapid accumulation of fluid, pericarditis and pleuritis occurring more commonly than peritoneal involvement.

Cardiac Signs

The cardiac manifestations relate to the pericardium (acute pericarditis and pericardial effusion), to the myocardium, and to the endocardium. The endocardial lesions were described by Libman and Sachs, the so-called *verrucous endocarditis.* A mitral systolic murmur may appear. Gallop rhythm may be heard. With myocardial damage, changes in the T waves and RS-T segments may be recorded with low amplitude of QRS complexes and prolongation of the P-R conduction time Heart failure may occur. The pericarditis may be serofibrinous, leading to obliteration of the cavity. The usual signs and symptoms of acute pericarditis—pain, friction rub, and elevation of the RS-T segments in all leads going on to negativity and coving—may be recorded. Fluid may accumulate rapidly and give rise to cardiac tamponade. With rise in venous pressure, râles may collect at the lung bases, and pleural effusion may form The liver becomes enlarged and tender, and edema appears.

Renal and Skin Lesions

With kidney damage there may be red blood cells in the urine The typical lesion in the kidney is the wire loop appearance of the glomeruli. Azotemia and rise in blood pressure do not usually occur. There are usually skin lesions, the typical one being the so-called "butterfly" rash across the nose The skin manifestations are prone to appear or be exacerbated after exposure to sunlight. Papular and erythematous eruptions also appear on other parts of the face, chest, and upper and lower extremities. They have a bluish cast and may scale Erythematous lesions may appear in the buccal mucosa and may ulcerate.

Treatment

Until recently there have been no drugs which altered the course of the disease in any significant way. The treatment has been symptomatic, with therapy of the individual manifestations by whatever means were available. Recently ACTH has induced prompt remission with fall in temperature, clearing of joints, and recession

of pericardial and other manifestations, and disappearance of the proliferations of connective tissue within a matter of hours There may be rise in blood urea nitrogen and in blood pressure. At present this drug appears to be a tool more for study than for therapeutic purposes How long remissions will last, and whether a dosage can be given without the disadvantageous side effects—rise in blood pressure, masculinization, growth of hair and beard, moon-shaped face, and appearance of other manifestations of Cushing's syndrome—remains for future work Cortisone has also been used with transient benefit

Acute pericarditis is treated by the usual measures which provide symptomatic relief If the pericardial effusion is large, removal of fluid by tap may be required Heart failure is treated by appropriate measures.

ECHINOCOCCUS CYST OF THE HEART

Cardiac Manifestations

Echinococcus cysts of the heart have been diagnosed during the life of the patient. The most common location of the cyst is in the right side of the heart, the right ventricle being more commonly implicated than the right auricle This right-sided frequency is attributed to the fact that the right coronary artery is more direct than the left The dog tapeworm infection (*Taenia echinococcus*) may occur early in life but cysts will not be found until twenty or more years later Diagnosis is possible if roentgenograms of the chest show the cyst with calcification in its wall There may be eosinophilia, intradermal skin tests with echinococcus antigens may be positive. There may be cysts in other parts of the body, for instance in the liver The electrocardiogram may be normal or show negativity and coving of $T_{1,2,4}$ like those seen in an old myocardial infarction The cardiac cyst may be dead or may be living There may be cysts on a pedicle projecting into a heart cavity. The cysts may rupture into the pericardial cavity or the heart cavities On rupture into the heart death may occur suddenly from anaphylaxis due to the entry of foreign protein into the circulating blood With the systemic distribution of the contents of the cyst embolic phenomenon may appear.

Treatment

There is no specific treatment for echinococcus cyst of the heart. When the location of the cyst appears appropriate for it, when there is no history that would suggest previous rupture, and when it is thought to be a single cyst, surgical removal has been successfully carried out If the patient has no symptoms operation may be postponed. It must be kept in mind that the constant motion of the heart predisposes to rupture

FRIEDREICH'S ATAXIA

Cardiac Manifestations

In this disease the heart may show widespread changes at autopsy. There may be enlargement of the heart caused by thickening of the muscle fibers and diffuse fibrosis. Pericardial effusion occurs. Microscopic examination shows fatty degenera-

tion of the muscle fibers with slight chronic inflammatory infiltration. Myocardial fibrosis and extensive coronary artery changes with obstruction have been reported. Involvement of the bundle of His may be inferred when auriculoventricular dissociation—which may be associated with Adams-Stokes syndrome—occurs. *In certain* patients the electrocardiogram may be of the T_1 type and in others of the T_3 type of deformity, in still others the T waves may be of low amplitude and inverted in all three standard leads. There may be increase in amplitude of the S waves which may be slurred. When several members of a family suffer from the disease they tend to show identical electrocardiographic changes. Angina may occur.

Heart Failure

When heart failure occurs, there is usually abnormality of the electrocardiogram. The likelihood of failure is also suggested by the degree of enlargement of the heart in x-ray photographs of the chest The prognosis is serious when there is complete heart block and Adams-Stokes syndrome.

TREATMENT. The treatment of heart failure is similar to that described in other patients suffering from this complication.

GALLBLADDER DISEASE AND CORONARY ARTERY DISEASE

Differentiation from Angina Pectoris

Differential diagnosis must occasionally be made between atypical gallbladder disease and atypical angina Under these circumstances even the visualization of gallstones may leave the diagnosis unsettled, because of the absence of collateral symptoms It is in cases such as these that the *anoxemia test* may be useful A positive result—especially if pain occurs which is similar to the spontaneous attacks —*may be taken as evidence that the spontaneous symptoms are due to coronary* insufficiency The exercise test, plus electrocardiograms, may give data which can be used in a similar fashion Frequent exhibition of electrocardiographic changes characteristic of coronary artery disease in the presence of gallbladder disease can be accounted for by the occurrence of the two diseases in the same age period, just as factors which were operative in the production of coronary artery disease might also account for the incidence of gallbladder disease. There are statistical data indicating that these two diseases are not closely related except through the influence of the aging factor.

Electrocardiographic Changes

Anginal attacks in man have been induced by distention of the gallbladder, as corroborative evidence of influence of the diseased gallbladder upon the production of angina Hodge and Messer have observed electrocardiograms before anesthesia, during distention of the gallbladder or common duct at operation, and during convalescence These patients complained of no symptoms of coronary artery disease which would indicate a previous myocardial infarction or the occurrence of angina pectoris. Disturbance in rate, rhythm, and T waves were seen, but the changes were thought to be insignificant. The investigators could not detect any electrocardiographic pattern of gallbladder disease, and the transient changes which were

observed did not suggest a coronary pattern. They state that conclusions regarding *improvement in the cardiac status of patients following gallbladder surgery are not* justified on the basis of single preoperative and postoperative electrocardiograms since serial electrocardiograms show instability of T waves.

Elective Surgery

Gallbladder disease occurs in patients who have undisputed evidence of impairment of the coronary circulation, not only with history of myocardial infarction but also with attacks of angina pectoris In them, activity of the gallbladder disease accounts for increase in incidence and severity of cardiac symptoms. If the functional capacity of the heart is not too greatly compromised and there is enough improvement in symptoms surgical treatment of the gallbladder disease should be considered It appears to be the safer course to perform an elective operation when the patient's condition is satisfactory.

GLYCOGEN STORAGE DISEASE

Definition

Glycogen storage disease, so-called Von Gierke's disease, is also known as *familial glycogen disease, cardiomegalia glycogenica* and *glycogenica conscripta*

This disease is due to the abnormal metabolism of glycogen resulting from a congenital defect and appears early in infancy As a consequence large accumulations of glycogen—which are fixed and cannot be mobilized by the body—are deposited in the organs, especially the liver and kidneys, and occasionally the cardiac and skeletal muscles, resulting in hypertrophy of the affected organs The liver or the heart may be predominantly involved The blood sugar is low without symptoms or hypoglycemia Occasionally, however, hypoglycemic-like attacks occur The disease may be familial.

Cardiac Manifestations

The symptoms of patients with cardiac involvement are not characteristic The infant fails to grow normally and is subject to respiratory infections There may be dyspnea and cyanosis; cardiac murmurs may be heard Those who survive to adolescence may show some improvement in their symptoms The heart may seem to be many times its normal size, it takes on a rounded appearance The ventricular walls are greatly thickened The heart muscle fibers are hypertrophied and contain large vacuoles which give a strongly positive glycogen coloring when stained with Best's carmine or with iodine stain Biopsy of skeletal muscle may give a clue to the diagnosis Liver biopsy may be done in the hepatomegalic type of the disease

Treatment

There is no specific treatment for glycogen disease Congestive heart failure may respond temporarily to the usual measures.

HIATUS HERNIA

Differentiation from Coronary Artery Disease

The symptoms of esophageal hiatus hernia, which is a type of diaphragmatic hernia, may simulate those of coronary artery disease, especially the anginal syndrome

There are frequent occasions when hiatus hernia must be considered in the differential diagnosis of precordial distress. It must be kept in mind that when a patient with a hernia is in the coronary artery disease age group separation of symptoms which might be attributed to the hernia and which to coronary artery disease may be difficult.

Types

Esophageal hiatus hernias may be present at birth or may occur at any time later. They are found in a large number of middle aged persons without their presence being suspected Three types are recognized. *Paraesophageal* hiatus hernia constitutes roughly one-quarter of the cases requiring surgical treatment The esophagus maintains its attachment to the diaphragm, and the cardiac end of the stomach herniates through the abnormal opening along the side of the esophagus. In the *second type the esophagus is shortened within the mediastinum but is long enough to reach the* diaphragm when traction is exerted, a type making up about three-quarters of those requiring surgical treatment. The hernias in these cases are larger than those of the first type. *In the third type of hiatus hernia there is a true short esophagus* of congenital origin with a partial thoracic stomach. These are not common.

Clinical Manifestations

Hiatus hernia may be present without giving rise to symptoms. The symptoms of esophageal hiatus hernia may be pain, epigastric distress, belching of gas, vomiting, palpitation, and dyspnea. Certain patients have difficulty in swallowing, especially of solid food, due to spasm, which may be relieved if they first take some fluid slowly. There may be difficulty in eructating gas. The substernal pain may be severe and radiate to the left shoulder, arm, or to the back. Jones thinks that overdistention of the bowel and of the esophagus or of the herniated portion of the stomach with or without associated gastritis or esophagitis is responsible for the production of the angina-like pain in the patients. He also thinks that small hernias are apt to mimic *angina pectoris in symptomatology*.

The symptoms may occur during or after a heavy meal, and may appear or be exaggerated by the prone position. The attacks last for a few minutes to several hours, at intervals of a week or a month, or more frequently. Symptoms usually [illegible] size. Frequently the symptoms are like those of [illegible] erosions. There may be anemia due [illegible] may occur.

Cardiac Symptoms

Dyspnea may occur from encroachment upon the pulmonary space. The function of the heart may be impaired by *displacement, rotation, and torsion.* Electrocardio-

graphic changes may be recorded because of displacement of the heart. Premature contractions may occur.

Visualization

Repeated fluoroscopic examinations and x-ray photographs may be required to demonstrate the presence of a hiatus hernia Tilting of the table and Valsalva tests are useful procedures.

Differential Diagnosis

An anoxemia or exercise test may be of use in differentiating hiatus hernia and angina (Chapter 12). Electrocardiographic changes are not known to occur during the pain of hiatus hernia, but hernial pain occurring in a patient who has an abnormal electrocardiogram may be temporarily confusing The absence of appropriate electrocardiographic changes, of rise in sedimentation rate and in temperature, and of fall in blood pressure would be evidences against the diagnosis of myocardial *infarction In some instances of hiatus hernia or when its presence is not precisely* demonstrated but suspected it may be useful to try the patient on a medical regimen.

Treatment

Medical Measures

The diet should be *bland Food should be eaten* in small amounts, *divided into* four to six feedings a day Nothing should be eaten before bedtime. Sleeping at an angle of 45 degrees may prevent symptoms An antacid such as aluminum hydroxide may be useful. Tincture of belladonna or atropine before meals may relieve spasm. The side effects of dryness of the mouth, tachycardia, and inability to accommodate for close vision may appear before effective dosages are obtained. The newer drugs of this series such as novatropine and trasentine do not cause these side effects and may be substituted Phenobarbital may be a useful adjunct Jones found that nitroglycerin gave relief in a few patients in the absence of any evidence of coronary artery disease.

Surgical Repair

Hemorrhage may require that surgical repair of the hernia be undertaken, especially if there is chronic loss of small amounts of blood Either the abdominal or the thoracic approach may be used Transient interruption of the left phrenic nerve by crushing and later by section, thus raising the diaphragm, may give relief to a certain number of patients with intractable pain. More recently relief has been afforded by pneumoperitoneum, which raises the diaphragm.

MYASTHENIA GRAVIS

Reports are at variance about the presence of myocardial lesions in myasthenia gravis. At any rate they are rare. Diffuse myocarditis and focal mural endocarditis have been described Other reports have recorded lymphocytic infiltration and *muscle fragmentation I have seen paroxysmal* auricular fibrillation. Attempts have been made to relate this disease to hyperplasia or to tumor of the thymus gland.

Weight is given to this notion since recovery or improvement have followed thymectomy in a few patients. The main therapeutic agent in the treatment of this disease is prostigmine. The early use of ACTH has been of benefit in certain patients.

MYOTONIA ATROPHICA

Clinical Manifestations

In myotonia atrophica, a familial disease usually appearing in early adult life, cardiac changes may occur. In this disease there is muscle atrophy associated with increase in muscle tone. There is early baldness, wasting of the temporal, facial, and sternocleidomastoid muscles so that the face has a masklike expression. Atrophy of the girdle and limb muscles occurs, causing patients to go through rather characteristic motions in the process of sitting up The increased muscle tone may be exhibited by having the patient shake hands forcefully, after which relaxation is delayed. This becomes less marked after the muscles have been used several times, as in making a fist quickly The tongue is dimpled when struck against a tongue depressor with a percussion hammer. Cataract and impotence are other characteristics

Cardiac Complications

The pulse is small, the blood pressure low. The electrocardiographic characteristics are prolongation of the P-R time (with duplication of the heart sounds), low amplitude of the P waves, splitting of the QRS complexes, and left axis deviation. The heart may be of any size, but is generally large if the P-R time is prolonged. Patients may complain of dyspnea without other signs of heart failure.

The heart muscle is also involved in *progressive muscular dystrophy*, but the changes may be less marked than in the skeletal muscles Patients may suddenly and without warning develop hypostatic pneumonia, pulmonary edema, hydropericardium, and hydrothorax, culminating in death The involvement of the heart muscle plays an important role in the terminal course of the disease The heart muscle at autopsy may show fibrous patches, the muscle is pale and flabby, with an increase in fat and interstitial tissue.

TREATMENT. The cardiac complications of these two diseases of muscle are accorded the appropriate therapy.

PERIARTERITIS NODOSA

Definition

Periarteritis nodosa (also called *polyarteritis nodosa* and *essential polyangeitis*) is a disease of unknown etiology characterized by widely distributed vascular lesions. The heart and kidneys are especially prone to damage. The disease is thought to result from a widespread hypersensitivity reaction. More recently the disease has been included among "diseases of the collagen system of the body." The disease was given its name by the early writers because of nodular enlargements along the course of peripheral arteries.

Clinical Manifestations

The small arteries in all of the organs of the body have been known to be involved, which accounts for the polymorphism of the symptoms and signs. It is usually a chronic disease, but may run a fulminating course. There may be remissions, but the course of the disease until recently has not been favorably affected by any known agents. The early manifestations depend upon which system or systems may be involved. The patient may give a history of asthma of a few years' duration —asthmatic râles may appear and disappear while the patient is under observation. There is usually rise in temperature, sweating, and tachycardia, polyarthritis with effusions into the joint cavities, and myalgia due to involvement of the vessels of the muscles. Urticaria, purpura, subcutaneous hemorrhages, and tender red nodules appear in the skin. Other serous cavities besides the joints are involved, especially the pleurae and pericardium; the pleurisy may be dry or may go on to effusion. A dry pericarditis or pericardial effusion may result. Adhesive pericarditis has been seen. With involvement of the coronary vessels, changes in the myocardium occur and heart failure may result. One of the characteristic groups of manifestations is that of peripheral neuritis, attributed to involvement of the vessels supplying the peripheral nerves. The renal vessels may be predominantly damaged so that there will be azotemia and rise in blood pressure Death may occur from uremia The typical blood picture is one of leukocytosis with eosinophilia and anemia. The leukocytosis may reach enormous proportions and cause confusion with myeloid leukemia

The cardiac manifestations may be related to pericarditis and to involvement of the coronary arteries. With hypertension the heart may enlarge and heart failure may occur.

Arterial Lesions

The typical lesion is characterized by inflammation and necrosis of the media and adventitia of medium sized arteries There is marked periarterial inflammation so that a nodule may form along the course of the vessel There may be marked eosinophilic cell reaction. The lumen of the vessel is encroached upon. There may be intimal damage with thrombosis of the vessel When large coronary arteries are implicated myocardial infarction may occur. With weakening of the necrotic arterial wall aneurysmal dilatations may follow, which may rupture and cause hematomas. Healing may be accompanied by fibrosis

Diagnosis

Bernstein made the first proved diagnosis of this disease before death by resorting to muscle biopsy The correct diagnosis has been more frequently made since the introduction of this procedure

The electrocardiogram may show the changes of acute pericarditis. There may be alterations indicating myocardial damage with lesions of the coronary vessels or there may be changes pointing to myocardial infarction when closure of a larger coronary vessel with thrombosis takes place.

Temporal Arteritis

Temporal arteritis is a variant of polyarteritis nodosa. The predominant lesion is of the temporal arteries, one or both being involved. It is characterized by fever, leukocytosis, eosinophilia, excruciating headache, and the appearance of nodules along the temporal artery. Surgical removal of the involved artery may be indicated.

Treatment

No form of therapy until recently has proved effective. The exhibition of ACTH has resulted in dramatic clinical improvement with prompt relief of asthma, anorexia, and asthenia, with fall in temperature and pulse rate. Whether patients with this disease can be cured with this drug in proper doses, or maintained in a state of remission on small doses or by intermittent therapy, has not yet been determined.

Acute pericarditis, myocardial infarction, and heart failure are accorded appropriate therapy. However, anticoagulant therapy should not be used for myocardial infarction because of the danger of aneurysms and their spontaneous rupture. Hemopericardium has resulted from rupture of aneurysm of a coronary vessel.

POLYCYTHEMIA VERA

Definition and Manifestations

Polycythemia vera or *erythremia*, also known as *Vaquez's disease* and *Osler's disease*, may be associated with cardiac and vascular complications. The cause of this disease, characterized by excessive red blood cell formation by the bone marrow, is unknown. It is associated with increase in circulating red blood cells, in viscosity of the blood, in the total circulating blood volume, and in the hematocrit reading of the blood. There is distention and engorgement of the capillaries with blood so that the patients have a red cyanotic color. The spleen may be enormously enlarged. The blood pressure may be moderately elevated. This form of polycythemia must be distinguished from the secondary polycythemia which is seen in congenital heart disease, chronic cardiovascular disease, Ayerza's disease, and chronic pulmonary disease.

The heart may be normal in size or slightly enlarged. Left axis deviation may be present in electrocardiograms, and occasionally right axis deviation. Heart failure may occur but is not common. Stewart, Wheeler, and Crane found that the cardiac output was diminished when the red blood cell count was elevated, but increased to normal levels with the reduction of the red blood cell count, or increased beyond normal if anemia was induced. There was a linear relationship between the number of red blood cells and the cardiac output. Although the cardiac output was decreased, the size of the heart was not appreciably increased, so that the work of the heart was commensurate with its size, which may have a bearing on the infrequency of heart failure in these patients. The reduction in cardiac output may be a com-

CARDIAC COMPLICATIONS

The most common cardiovascular complications of polycythemia vera are vascular thromboses and vascular hemorrhages. These may occur in any part of the body. Thrombosis of arteries and veins may occur spontaneously or be precipitated by phenylhydrazine. Coronary thrombosis is an occasional complication The association of polycythemia and hypertension without splenic enlargement has been described by Gaisbock as a separate syndrome, but it is likely that the polycythemia was secondary.

TREATMENT

When heart failure occurs it is accorded appropriate treatment. It may be safer to allow the patient to remain ambulatory than to run the risk of thrombosis from inactivity. Myocardial infarction may present special problems. If coronary thrombosis occurs it may be well, if the patient is not too sick, to allow more freedom of activity than would ordinarily be the case Bed rest for the usual four to six weeks would be shortened in appropriate cases to two weeks The advisability of anticoagulants in polycythemia has not been established. The temptation to use them is great, but in patients who are subject to spontaneous hemorrhages this additional hazard points to their avoidance. It is also thought by some that these patients are more sensitive to anticoagulants.

Patients suffering from this disease may be unusually sensitive to morphine. Maintenance of the red blood count within normal limits by venesection, x-ray therapy, and radioactive phosphorus prolongs the patient's life and may assist in the prevention of cardiovascular complications. The use of phenylhydrazine has waned with the introduction of radioactive phosphorus.

SARCOIDOSIS

DEFINITION AND CARDIAC MANIFESTATIONS

Boeck's sarcoid is a chronic infectious disease of unknown etiology with widespread systemic involvement skin, lymph nodes, bones, lungs, salivary glands, and occasionally the heart. The relationship to tuberculosis remains debatable.

Sarcoidosis may present cardiac complications because of involvement of the heart muscle and pericardium. Involvement of the lungs may be a cause of chronic cor pulmonale and heart failure.

Infiltration of the heart muscle may lead to cardiac decompensation. The cardiac lesions may be associated with fibrosis. Cardiac involvement has been the occasion for sudden death, the cause of which is not known, although the possibilities are ventricular fibrillation, defect in auriculoventricular conduction, or damage to the pacemaking centers

TREATMENT

The treatment of heart failure in this condition is similar to that carried out in other forms of cardiac decompensation. The use of ACTH is in the experimental stage. Prompt and marked improvement in pulmonary, cutaneous, lacrimal, parotid, and lymph node lesions has followed exhibition of this drug.

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SCALENUS ANTICUS AND CERVICAL RIB SYNDROMES

Definition

In the scalenus anticus and cervical rib syndromes symptoms occur which appear to be due to compression both of the brachial plexus and of the subclavian artery by the scalenus anticus muscle or a cervical rib, or by both. These symptoms are probably due to constriction by the scalenus anticus muscle in all instances, but they may be more readily brought out in the presence of a cervical rib. Nevertheless the syndrome occurs both with and—more frequently—without cervical ribs Short ribs may give rise to brachial plexus pressure, while long ones may give rise to subclavian artery compression.

Symptoms

Pain

The symptoms depend on the structure involved. Pain, which may be sharp or dull, is the most common symptom. It may resemble that of angina pectoris. It may follow the course of the ulnar and median nerves, or extend up into the shoulder or neck. The pain may be continuous but exaggerated by rotation of the head or by using the arm as in sweeping or dusting. There may be numbness, paresthesia, hyperesthesia, and anesthesia after sleeping or working with the arms in the position of hyperabduction. At a later stage atrophy, chiefly of hand muscles, may occur

Compression of the Subclavian Artery

Vascular symptoms may be associated with varying degrees of compression of the subclavian artery, or they may be due to organic change in the vessel or its branches which may advance to actual occlusion with edema, cyanosis, and gangrene Compression may cause an aneurysm of the vessel. Other vascular symptoms are due to disturbances of the sympathetic system, with vasomotor changes simulating Raynaud's disease.

Diagnosis

In certain patients fullness in the neck may be detected on palpation in the region of the cervical rib Roentgenograms may be required. Change in position of the arm may induce alterations in volume of the radial pulse and perhaps lead to its obliteration; taking a deep breath during these maneuvers may accelerate the decline in pulse volume These changes may be more readily detected if the blood pressure is taken in addition to palpation of the pulse.

It is likely that differences in tension of the scalenus muscle as well as other factors may be important in the production of symptoms Symptoms may be referred to one or both arms Trauma or occupational posture may be precipitating factors.

Wright has described symptoms in patients due to hyperabduction of the arms which are similar to those in these two syndromes.

Treatment

Improvement in posture may provide relief. On the other hand if the symptoms are severe and persist, excellent results have been reported following scalenectomy. In order to assure the nerve and artery of an unimpeded course, partial or complete removal of the rib may be necessary; if any rib is left in place, regeneration may lead to recurrence of symptoms. The operation may be performed under local anesthesia.

Alterations of the volume of both radial pulses up to their obliteration, with pain and numbness in both hands, resulted from progressive deformity of the chest in a young man I have seen recently with funnel chest. In this patient pain due to compression was persistent when the arms were hanging down at his sides. The patient learned to get some relief by keeping his shoulders raised. Bilateral scalenectomy resulted in relief of symptoms.

When pain results from sleeping with the arms hyperabducted, change in the position of the arms brings relief of symptoms. When the hyperabduction syndrome is occupational and persists after change in occupation, scalenectomy may be required. In other instances removal of a part of the clavicle may be necessary.

SCLERODERMA

Pathology

Myocardial involvement in scleroderma may be the cause of congestive heart failure. Although uncommon, several cases have been recorded in the literature. The cardiac symptoms may precede the skin changes. The lesions are characterized by areas of fibrosis without inflammatory reaction. In some instances remnants of muscle fibers may be seen in the center of fibrotic areas Large amounts of cardiac muscle may be replaced by this fibrous tissue The coronary vessels may be intact or the small vessels may show thickening. In other cases endocardial and pericardial lesions have been described.

Clinical Manifestations

There may be prolongation of the P-R conduction time, progressing to complete heart block. Auricular fibrillation may occur. The heart is enlarged, the enlargement being for the most part due to dilatation. Patients may complain of precordial distress, which may be confused with the symptoms due to hiatus hernia, present in a good proportion of patients with esophageal lesions. Congestive heart failure may be the cause of death.

Treatment

The treatment of the heart failure in scleroderma is similar to that in other types of congestive heart failure The benefit may not be marked and death may occur within a few months ACTH has been used experimentally in a few cases with temporary improvement.

SERUM CARDITIS

Pathology

Experience with Animals

When in 1915 Longcope injected rabbits with foreign protein, the structural cardiac changes observed included perivascular granulomata, areas of necrosis, cellular infiltrations, and endothelial proliferation around the smaller coronary arteries. Boughton repeated these observations two years later and a number of other investigators described changes in the hearts of anaphylactic animals. In 1931 Criep described electrocardiographic changes in guinea pigs in anaphylaxis, which were attributed to myocardial ischemia In 1937 Wilcox and Andrus reported similar changes in the isolated hearts of guinea pigs, previously sensitized to horse serum, when the perfusion medium contained the horse serum antigen. In addition there was diminution in the rate of coronary blood flow.

Experience in Humans

In 1937 Clark and Kaplan reported three instances of carditis in patients with serum sickness The structural changes observed at postmortem included proliferation of histiocytes in the mural and valvular endocardium and in the intima of the coronary arteries, and stimulation of mesenchymal tissue of the myocardium.

In 1940 Wadsworth and Brown reported a case of hypersensitivity reaction in a previously healthy youth twenty-four hours following 5 cc. of horse serum containing antitoxin against tetanus and gas bacillus. The clinical and electrocardiographic changes were indistinguishable from those seen in active rheumatic carditis and consisted of low amplitude and splitting of the QRS complexes, prolongation of the P-R interval, and RS-T wave changes of a nonspecific character The subsequent course was that of acute rheumatic fever

In 1942 Fox and Messeloff reported another case of serum carditis in serum sickness due to tetanus antitoxin This was accompanied by electrocardiographic deformities like those of the previous report Rich in 1942 again described structural alterations in the myocardium in the hypersensitive state These changes were thought to be indistinguishable histologically from the myocardial lesions of rheumatic fever.

Cardiac Signs and Their Treatment

The cardiac manifestations which commonly simulate those of rheumatic carditis are accorded appropriate therapy. In one patient we have seen with electrocardiographic changes pyribenzamine was used in the treatment of the serum sickness.

TRICHINOSIS

Cardiac Manifestations

In trichinosis there may be clinical and electrocardiographic evidence of myocardial involvement. The so-called "trichinal myocarditis" is due to the presence of larvae in the myocardium and to their migration, and not to a blood-borne toxic

substance. The electrocardiogram goes through a series of changes reflected in Leads II, III, and IV, with negativity and coving of the T waves. From the widespread distribution of the larvae one would not expect a characteristic pattern. There may be lowering of the amplitude of the QRS complexes and intraventricular block. Transient prolongation of the P-R conduction time may occur. The changes, when detected in serial electrocardiograms, record the migration of the larvae into the heart muscle. In patients dying of trichinosis there may be necrosis of muscle fibers and infiltration with leukocytes and larvae may be seen in sections of the heart muscle Other vascular manifestations are congestion and hemorrhages of the conjunctivae and sclerae, hemorrhages of the gastrointestinal tract with bloody diarrhea, edema, especially of the eyes and face, peripheral venous thromboses, embolism with infarction, and hypotension Fresh thrombi have been found in the auricles at postmortem examination. Death between the fourth and eighth week of infection may result from myocardial damage Detection of larvae in the eyegrounds confirms the diagnosis before the muscle biopsy is processed.

Treatment

Patients should remain in bed until fully recovered from the trichinal infection. ACTH has been used in a few patients. When heart failure occurs it is treated by the usual measures

TUMORS OF THE HEART

Types

Tumors of the heart may be primary or secondary. they may arise in the heart itself, or they may be metastatic to the heart from other primary foci *Primary* tumors of the heart are rarer and are not often diagnosed with certainty, metastatic involvement can be detected more commonly In either case treatment must in most cases be confined to the symptomatic.

Tumors Metastatic to the Heart

Metastases to the heart have been reported from neoplasms—particularly carcinomas or sarcomas—of all the main organs.

With involvement of the pericardium, there may be a pericardial friction rub, and signs of pericardial effusion and tamponade requiring pericardial tap may occur The electrocardiogram may give the first evidence of pericardial metastases Tumor cells may be detected in the pericardial fluid. Additional signs may be unexplained heart failure and the occurrence of abnormal rhythms, such as paroxysmal ventricular fibrillation and auricular flutter and fibrillation Metastases may give rise to thickening of the pericardial sac, obliteration of the cavity, and involvement of the visceral pericardium, and may result in the clinical picture of cardiac compression, in short, they may produce the Pick syndrome Metastases may also be located in the substance of the heart muscle

Primary Tumors

Primary tumors may be benign or malignant. For some reason yet unexplained, the most common location of benign tumors is in the left auricle, the left ventricle

being the second in frequency, while malignant tumors are most frequently found in the right auricle. Congenital cysts of the myocardium have been reported.

Myxoma

Myxoma is the most common primary cardiac tumor and arises most often from the endocardium of the left auricle. It is pedunculated and may, by a ball valve action, plug the mitral orifice. When this occurs there may be history of fainting with convulsions, especially on standing. There may be inconstant or changing signs of mitral stenosis.

Fibroma

Fibromas are also endocardial, and arise from the subendothelium of the valves tricuspid, aortic, mitral, pulmonic, in order of frequency. They may be myxomatous.

Sarcoma

Sarcomas arise most frequently in the right auricle, less common sites are the left auricle and the pericardium They metastasize. They may be large and pedunculated and encroach upon the cavities of the heart. All the common varieties of sarcoma have been reported. There may be progressive onset of heart failure, pericarditis, obliteration of the pericardial cavity with neoplastic tissue, electrocardiographic changes with negativity of $T_{1, 2, 3}$, and prolongation of the P-R conduction time up to complete heart block. Idiopathic hemorrhagic sarcoma—so-called Kaposi's disease—has supplied a tumor of the right auricle with onset suggesting a respiratory infection

In rhabdomyomas the muscle cells may be tubular and contain vacuoles. Congenital rhabdomyomas of the heart may be associated with other cardiac developmental defects and with feeble mindedness or epilepsy The rhabdomyoma may be solitary at the apex or multiple with subendocardial, intramuscular, or subepicardial locations, and may or may not project into the cavities of the heart or pericardium. In other instances the lesions may be diffuse

Other Tumors

Lipoma, lymphangioendothelioma, and hemangioendothelioma have been reported. Primary endothelioma of the inferior vena cava with propagation upward into the right auricle and right ventricle has ruptured into the pericardium and caused death In this case alteration of the QRS complexes occurred The angiomas, as elsewhere in the body, develop rapidly and destroy tissue. Heart failure occurs and complete heart block has been reported from septal involvement. Varices of varicose veins, blood nodes, or blood cysts occur most commonly in the right auricle, on the rim of the fossa ovalis.

Diagnosis of Cardiac Tumors

Although cardiac tumors are not diagnosed frequently there are a few clinical [illegible] tumor of the heart: (1) Heart [illegible] or, such as signs of valvular [illegible] body, and fainting due to [illegible] blocking of the mitral orifice by a pedunculated tumor; (3) onset of heart failure

and cyanosis, especially in a patient with known malignant disease; (4) signs of pericarditis with friction rub and accumulations of hemorrhagic fluid in the pericardium and pleura from which tumor cells may be recovered; (5) roentgenograms may show suggestive changes in the contour of the heart or give evidence of pericardial and adjacent lymph node involvement.

The occurrence of paroxysmal rhythms may afford a clue which should not be ignored. In the presence of primary or secondary tumors the electrocardiographic changes are like those seen in acute pericarditis. The abnormalities in T waves differ from those seen in coronary thrombosis, in that T_1 and T_3 are not reciprocal and upward displacement of the RS-T segments occurs. Intracardiac tumors may give a clinical picture simulating Ayerza's disease, mitral stenosis, and pulmonary stenosis.

Yater states that hemorrhagic pericardial fluid is highly presumptive evidence of tumor of the heart; it is not uncommon, however, for tuberculous pericarditis also to give rise to a serosanguineous effusion

Treatment of Cardiac Tumors

When metastatic implantation of the heart and pericardium has occurred, the primary disease is too widespread to accomplish much in the way of long-term treatment If pericardial effusion occurs and gives rise to tamponade, pericardial tap may be required Heart failure and cardiac arrhythmias are treated in the appropriate manner.

Radiotherapy may be attempted if the primary tumor is radiosensitive. Shelburne and Aronson report the use of deep x-ray therapy in a patient with metastatic pericardial involvement and complete heart block due to septal development There was regression of block to 2:1 ratio, then restoration of normal rhythm and decrease in size of the heart, with temporary improvement of the patient so that he was able to return to work The patient, however, finally died of mediastinal compression It is to be kept in mind that x-ray and radium therapy, and the use of radioactive substances in the presence of pericardial involvement may lead to constriction of the heart by shrinking of tissues and fibrotic changes and give rise to the picture of chronic constrictive pericarditis

With the recent, more daring trends in cardiac surgery, if a single primary tumor of the heart should be diagnosed, exploratory operation might be attempted The perfection of the mechanics of maintaining an extracorporeal circulation will facilitate the surgical treatment of cardiac tumors. Beck has successfully removed a calcified cyst of unknown type from the heart in the region of the left ventricle.

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CHAPTER 19

Acute Myocarditis

INTRODUCTION

The term acute myocarditis was formerly used widely and without great accuracy There followed a period in which this diagnosis was not made often as a clinical entity. Careful autopsy examinations have shown, however, that the myocardium may be damaged by a large number of agents, although the lesions, as well as the effects on the functional capacity of the heart, are more or less similar

ETIOLOGIC AGENTS

Among the organisms which may cause acute myocarditis are the meningococci, the gonococci, and the microaerophilic streptococcus hemolyticus Among the diseases in which acute myocarditis occurs are diphtheria, typhoid and paratyphoid fever, pneumonia, scarlet fever, tularemia, streptococcic and meningococcic meningitis, and acute tonsillitis. It has occurred in bronchiectasis, in exfoliative dermatitis associated with laryngeal edema in children, in acute nasopharyngitis, and in subacute bacterial endocarditis

Cases of acute myocarditis have been reported in the following virus infections: poliomyelitis, influenza A, mumps, scrub typhus, Rocky Mountain spotted fever, typhus, yellow fever, psittacosis, measles, smallpox, and chickenpox.

Acute myocarditis has been recorded after the use of *sulfonamide drugs*. In large amounts *digitalis* has been shown to induce myocardial damage in animals, but thus far cases in humans have not been reported.

CLINICAL PICTURE OF BACTERIAL AND VIRAL MYOCARDITIS

In acute myocarditis due to bacterial or to viral agents the clinical picture and history are more or less similar It may occur at any age but is more common in young persons. A patient with one of the diseases listed under Etiologic Agents

who might be thought to be going on very well, dies suddenly without any premonitory signs, or sudden death may occur shortly after the onset of signs and symptoms of cardiac involvement. There may be sudden heart failure, substernal oppression, angina, palpitation, cyanosis, dyspnea, or orthopnea. The heart rate increases and may be out of proportion to the temperature curve. The blood pressure falls and the pulse becomes feeble and thready. There may be marked asthenia. There may be gallop rhythm or other cardiac arrhythmias The sedimentation rate may be rapid A wide variety of electrocardiographic changes may occur. prolongation of the P-R conduction time, alteration of the T waves with negativity and coving, RS-T segmental changes, lowering of the amplitude and splitting of the QRS complexes, and bundle branch block. The heart may increase in size.

No doubt many cases occur which are mild and are not recognized. Many of the recognized cases recover. Acute myocarditis may be confused with coronary thrombosis, acute pericarditis, and acute rheumatic myocarditis. The diagnosis is made by exclusion.

CASES OF UNKNOWN ETIOLOGY

Some cases of acute myocarditis are of unknown etiology Although there is no antecedent disease, patients show clinical pictures similar to those with known preceding disease, including the electrocardiographic changes. Probably most of these patients recover.

Fiedler's Myocarditis

In this group is a number of cases in which the outcome is fatal within a matter of months. Death may occur suddenly, it may be the result of heart failure In some patients there have been embolic phenomena. The heart is enlarged. Low amplitude and splitting of the QRS complexes of the electrocardiogram, and bundle branch block are common There may be a septic type of fever.

The lesions may be diffuse, isolated, or granulomatous, and differ from those seen in septic myocarditis Many areas of the heart muscle should be examined if the lesions are not to be overlooked. It is noteworthy that the endocardium or pericardium are not generally involved The changes may be principally interstitial, but the heart muscle fibers may be involved and show degeneration, fragmentation, and necrosis, older lesions may show fibroblasts and, later, fibrosis There may be new blood vessels Lymphocytes and macrophages are the most common cellular elements, but polymorphonuclear and eosinophilic cells may be seen.

Cases Described by Smith and Furth, and by Dock

Finally, there are the two groups of cases described by Smith and Furth, and by Dock, which were characterized by large hearts, cardiac failure, elevated venous pressure, prolonged circulation time, low amplitude and splitting of the QRS complexes, bundle branch block, and *mural thrombi* with repeated *embolic phenomena*, especially pulmonary infarcts, occurring in patients with an alcoholic history or with severe dietary deficiency. Attempts have been made to relate these cases to Fiedler's myocarditis and to beriberi heart disease. The most marked feature in all

cases was the widespread endocardial fibrosis in both right and left ventricles, which, with the heart failure, predisposed to mural thromboses with emboli. Vascular and valvular changes were absent.

TREATMENT

The characteristics and treatment of acute myocarditis found in active rheumatic infection is described in Chapter 7. In other cases of the disease the patient should remain at complete bed rest. With the onset of heart failure the usual measures are employed The patient is promptly digitalized in an attempt to increase the efficiency of the undamaged part of the heart muscle. Toxic effects should be avoided carefully. The low blood pressure, tachycardia, and feeble pulse may simulate shock. This state results from myocardial failure and not from peripheral circulatory failure, and intravenous fluids may be lethal to the failing heart. Bed rest should be continued until the sedimentation rate is normal, and until the electrocardiogram has either returned to normal or become stabilized. Mobilization should be slow.

In many cases of Fiedler's myocarditis the presenting features are a large heart, bundle branch block, and congestive heart failure with no obvious etiologic basis. All the measures employed in the treatment of congestive heart failure may be required.

For patients presenting the syndrome described by Smith and Furth, adequate amounts of vitamin B may be supplied in addition to the measures usually employed in the treatment of heart failure. If embolic phenomena such as pulmonary infarction occur, heparin and perhaps dicumarol may be used.

The treatment of *diphtheritic myocarditis* requires special consideration. This complication may arise when the patient is apparently well on the way to recovery. The early administration of antitoxin intravenously, diluted with saline, goes far toward the prevention of myocarditis. The shocklike state may be a manifestation of myocardial insufficiency and too vigorous use of intravenous fluids may be fatal. Epinephrine, norepinephrine or neosynephrine should be used if there is a fall in blood pressure. Vasomotor paralysis may be sudden, with disturbed peripheral circulation, relaxed splanchnic vessels, and oliguria. An abdominal binder may be used and the foot of the bed raised One hundred to five hundred cc. of 10 per cent glucose are given intravenously, depending on the age of the patient, the amount being increased up to 1000 cc. in 24 hours in adults. Digitalis is not beneficial in this state of the circulation; indeed it may be harmful. Late myocardial changes occur in the first or second week of the disease. At this time conduction changes may be detected in electrocardiograms and heart failure may appear. Under these circumstances digitalis may be used cautiously. The patient should remain in bed until the electrocardiogram is normal or, in the case of conduction defects, until heart block becomes established or disappears. Bed rest may be required for six to eight weeks if there are electrocardiographic changes, and for four to five weeks if these are not demonstrated

Myocardial involvement may be shown in the electrocardiogram in diphtheria without any clinical evidence of heart disease. They may be reversible and shift

from day to day. They may be toxic in origin, not due to structural damage. The changes are characterized by decreased amplitude of the T waves which may show negativity and coving, and by RS-T segmental depression.

SUMMARY

It is apparent that a wide variety of agents—bacterial and viral, as well as some unknown agents—may result in damage to the myocardium, giving a picture which is recognized as acute myocarditis when sections of the heart muscle are examined after death. No special features are known to distinguish the etiologic agents microscopically. The essential clinical features suggesting acute myocarditis, which are varied, have been described. The treatment of acute myocarditis is symptomatic with the use of the full complement of measures when there is heart failure.

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CHAPTER 20

Diseases of the Pericardium and the Mediastinum. I. Acute Pericarditis, Pericardial Effusion, and Other Entities

ACUTE PERICARDITIS

Pathology

Acute pericarditis may result from inflammation of the pericardium by infectious agents or by irritation of its serous surface. The inflammatory reaction may appear first either on the visceral or the parietal pericardium and involve the pericardial sac Pericarditis may either be dry with a to-and-fro pericardial friction rub synchronous with systole and diastole, or varying amounts of fluid may accumulate within the pericardial cavity. When fluid accumulates rapidly the pericardial sac does not stretch easily and tamponade appears quickly If fluid accumulates slowly the pericardium stretches and larger amounts of fluid may be accommodated with the slower development of signs of compression of the heart and of embarrassment of the mechanical ability of the heart. The fluid may be a transudate or an exudate. It may be serous or serosanguineous, it may be thin in streptococcal infections, thick in staphylococcal and pneumococcal infections

Clinical Manifestations

Patients who have acute pericarditis of infectious origin usually appear ill. This is particularly the case if pericarditis is due to active rheumatic fever, to tuberculous, pneumococcal, staphylococcal and streptococcal infections, and other known or unknown infectious agents. In a setting of an acute respiratory infection, however, the involvement of the pericardium may not be severe and might be unrecognized if electrocardiograms and x-rays of the chest are not recorded.

LEAD I LEAD II LEAD III LEAD IV

4- 1-48

5- 5-48

6-11-48

9-17-48

9-24-48

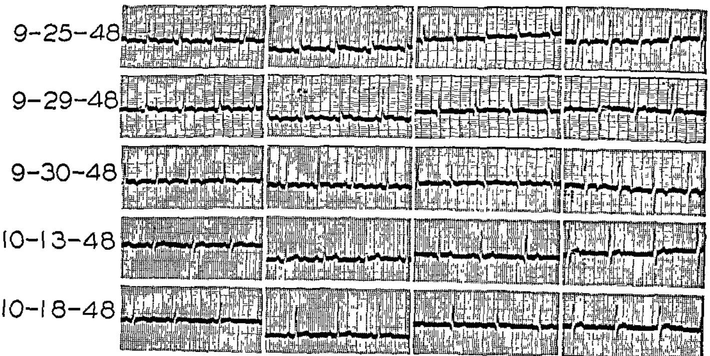


FIG 45.

Electrocardiograms from a Boy 16 Years of Age, during Three Bouts of Acute Pericarditis within a Few Months Etiology was unknown, but may have been due to rheumatic fever although there were no other evidences of rheumatic activity in the past or during these episodes

April 1, 1948, negativity and coving of the T waves in Leads I and IV and an abnormality of T_2 which with the large heart shadow and increase in venous pressure were interpreted as being due to acute pericarditis with effusion There was reversion to approximately *normal configuration of the* T waves in Leads I, II, and III by the *time the electrocardiogram was taken on May 5, 1948. Later there* was recurrence of evidence of acute pericarditis and in the electrocadiogram taken on *June 11, 1948* T_1 was again negative and coved, *T_4 was deeply negative and coved*, and T_2 was of decreased amplitude and had changed *its* contour

In September, *1948*, the patient's electrocardiograms went through another series of changes with clinical evidence of acute peri*carditis as shown in the electrocardiograms Early* there was elevation of the RS-T segments going through progressive changes to negativity and coving, after which the T waves became upright

There is usually fever, its height varying with the severity of the infection Patients complain of precordial pain, which may be aggravated by deep respiration. Dyspnea may be marked, with respirations of the short gasping type. The pericardial friction rub may be typically to-and-fro or may be heard only in systole; it may be transient or may persist; and may be accompanied by a friction fremitus. Varying grades of leukocytosis are recorded which depend upon the offending organism The sedimentation rate is elevated. The electrocardiogram may show the evolution of changes which are typical of pericardial involvement (Fig. 45). The acute phase varies with the causative agent. Recovery may be complete without residual pathologic changes, or fibrous strands may form between the visceral pericardium and the pericardial sac which usually do not give rise to any functional disturbance of the heart. These may be found later at autopsy following death from some other disease. On the other hand the visceral and parietal pericardial involvement may be such that the pericardial cavity may be obliterated and signs of chronic constrictive pericarditis appear. In other instances adhesive pericarditis results without the occurrence of signs of compression—a sequence of events which may follow rheumatic pericarditis.

In some patients, fluid may form without the dry stage having been recognized With the appearance of fluid the friction rub may disappear or may be heard only when the patient lies in certain positions The fluid may form slowly or rapidly as in streptococcal infections. Dyspnea and urgency of breathing become more marked, cyanosis may appear; the area of percussion dullness increases, the heart sounds become fainter, the blood pressure falls, the pulse pressure decreases, and the cardiac shadow increases in x-rays. Varying components of cardiac tamponade may be seen. The compression of the heart may occur so rapidly or be so marked that decompression of the heart by pericardial tap is urgently required. Venous engorgement appears; râles at the lung bases or pleural effusion may be seen; the liver may enlarge, and ascites and edema may be apparent. The amount of pericardial fluid, however, may be so small that its presence cannot be detected without x-ray photographs of the chest.

Visualization

Angiocardiography may aid in the diagnosis of pericardial effusion by delimiting the borders of the heart and differentiating the cardiac chambers.

Electrocardiographic Changes

In acute pericarditis the electrocardiogram may undergo a series of characteristic changes early there is elevation of RS-$T_{1,2,3,4}$ but changes may be confined to RS-$T_{1,2,4}$ (Fig. 45). The take-off is straight and without the rounding seen in early myocardial infarction. Over a period of several weeks later these segmental elevations work their way downward and coving begins, resulting in negativity and coving of $T_{1,2,3,4}$, $T_{1,2,4}$ (Fig. 45), or of $T_{2,3}$ The abnormality of the T waves may persist for many months or years before gradual regression takes place. When effusion occurs the electrocardiographic pattern does not differ from that seen in acute pericarditis except that the QRS complexes may decrease in amplitude and increase again with disappearance of fluid. However, if the pericardium thickens

and constrictive pericarditis occurs with the absorption of fluid, the QRS complexes may decrease further in amplitude. Patients may have repeated episodes of acute pericarditis with electrocardiographic changes with each (Fig. 45). Fluid may be absorbed without any permanent damage to the pericardial sac or cavity.

The electrocardiographic pattern seen in acute pericarditis may be duplicated if pericardial irritation occurs from any cause whatever, such as leukemic infiltration or metastases from tumors. Such electrocardiographic changes have been attributed to extension of the irritative or inflammatory process to the myocardial layer immediately beneath the visceral pericardium.

The sequence of acute pericarditis with effusion and resorption may take place in a matter of days or over a period of months There may be recurrences while the patient is improving. In some instances it is surprising how rapidly the fluid may undergo resorption. With recovery the temperature falls to normal, the evidence of effusion or dry pericarditis disappears, and the patient's clinical condition improves. The sedimentation rate may fall with recovery or may remain elevated for some period of time afterward.

Pathologic Physiology

As pericardial fluid accumulates the heart is compressed so that it is unable to relax in diastole sufficiently to admit a full quota of blood Consequently it expels a smaller amount of blood with each systole, thus decreasing the volume output of the heart, while the venous pressure rises and the circulation time becomes prolonged When the signs of cardiac tamponade appear the heart rate increases, the blood pressure falls, and pulse pressure declines and the pulse becomes paradoxical, decreasing with inspiration and increasing with expiration, in contrast to behavior of the radial pulse in most normal subjects Unless the variation is marked, a paradoxical pulse is more easily detected while taking the blood pressure than by palpation of the radial vessel If the pressure in the blood pressure cuff is set so that it remains at the systolic level during auscultation over the antecubital space, the sounds disappear during inspiration and reappear during expiration if the patient breathes slowly and deeply.

The compression of the lung by the distended pericardial sac at the angle of the left scapula usually indicates a large effusion Following the size of the heart by percussion and in x-ray photographs of the chest affords a guide to the rapidity of the accumulation of fluid and state of distention of the pericardial sac

Venous stasis can be seen in infrared photographs of the body. As a consequence of the venous engorgement, enlargement and tenderness of the liver, râles in the lungs, pleural effusion, edema, and ascites may appear. These signs regress with absorption of pericardial fluid and may disappear entirely. If, however, the pericardial cavity is obliterated and the pericardium becomes thickened and perhaps later calcified and constricts the heart, signs of obstruction and of chronic constrictive pericarditis reappear Adhesive pericarditis may result from acute rheumatic pericarditis but constriction of the heart does not occur External adhesions to the anterior chest wall and cardiac enlargement resulting from valvular disease prevent constriction of the heart.

TREATMENT

General Measures

The underlying disease is treated as may be indicated. Pain associated with pericarditis may be lessened by an ice bag. In addition aspirin, codeine, and morphine may be required. When dyspnea is marked, oxygen by tent or mask may give relief. When the signs of tamponade indicate a marked compression of the heart, pericardial tap may be required to remove some of the fluid (pp. 409-410). Although the signs due to cardiac tamponade may cause the patient to appear to be in heart failure, digitalis is contraindicated. Under these circumstances digitalis would be expected to decrease further the size of the already compressed heart and would thereby decrease the already compromised cardiac output.

Pericarditis Associated with Active Rheumatic Fever

The treatment of the pericardial manifestations of active rheumatic fever, namely acute pericarditis and pericardial effusion, has been discussed in Chapter 7.

Tuberculous Pericarditis with Effusion

Tuberculous pericarditis occasionally occurs as a low-grade infection which will go undetected until signs and symptoms of constrictive pericarditis appear. Calcification may or may not be demonstrated Some of these cases give no clinical history of any episode which could be interpreted as acute pericarditis At operation the typical microscopic picture of tuberculous infection may be seen in the resected pericardium Cure of the syndrome may be achieved with complete recovery and without recurrences or may be apparently accomplished only to have the patient succumb later to tuberculous infection elsewhere in the body.

More frequently, however, tuberculous pericarditis with effusion is acute and the patient is very sick, the mortality rate being around 80 per cent. An overwhelming tuberculous infection may occur; the pericarditis may present the main defect but pleural and peritoneal surfaces are involved as well. The pericardial fluid may be hemorrhagic. Miliary tuberculosis with marked involvement of the lungs is *not uncommon in such a clinical picture This form of infection is more common* in Negroes.

ACUTE PHASE. The usual measures are employed ice bag to precordium for pain and sedation as needed. When tamponade occurs and respirations are labored and short and panting, pericardial tap is indicated (see p. 409 for technic). Fluid, which may be serous or serosanguineous, is removed slowly in order not to precipitate cardiac dilatation It may reaccumulate rapidly so that repeated taps are required. Examination of the pericardial fluid, the sputum, and stomach washings for tubercle bacilli, and demonstration of tuberculous lesions of the lungs in roentgenograms may establish the diagnosis. When the diagnosis is established the administration of dihydrostreptomycin or isonicotinic acid hydrazide should be considered. Since most instances of proved clinical tuburculous pericarditis at this stage are fatal, these drugs should be given a trial.

CONTINUED TREATMENT. The patient is given the usual treatment for tuberculosis. The treatment of acute tuberculosis pericarditis with effusion by pneumo-

pericardium or by the injection of air and lipiodol into the pericardial cavity has not been effective Blalock has advocated pericardiectomy for patients in the acute stage of acute tuberculous pericarditis with constriction of the heart, being of the opinion that mortality was thereby lowered. More recently Holman and Willett reported that five patients treated in this manner were benefited.

Acute Pericarditis of Unknown Etiology

Acute pericarditis may occur after acute respiratory infections. In many such instances culture of the pericardial fluid on all the known media fails to isolate any known organisms. The etiology has to be listed as "Unknown." Some of these patients recover without any after-effects. A number of them, however, later develop the syndrome of chronic constrictive pericarditis. For this reason patients with acute pericarditis should remain at rest in bed until the temperature, sedimentation rate, and white blood cell count have all returned to normal levels; until stabilization of the electrocardiogram has occurred, and until it is certain that tamponade or constriction of the heart are not imminent The general measures appropriate for the treatment of acute pericarditis are employed. Since a specific organism cannot be implicated, antimicrobial therapy may not at present be useful. If there is fever and the patient is acutely sick aureomycin or chloramphenicol, and perhaps penicillin or terramycin may be used These cases should be followed for many years to detect the appearance of Pick's syndrome, which we have seen evolve in some patients

Viral Pericarditis

When serial electrocardiograms and serial x-rays of the chest detect contributory evidence of acute pericarditis during a viral infection no special therapy is required unless the amount of fluid is so large that it must be removed by tap Aureomycin or chloramphenicol may be effective Complete rest in bed is advised until all evidences of infection have disappeared Mobilization is gradual Occasional observations, including electrocardiograms, are indicated in order to follow the restoration of the normal contour and to be prepared for the appearance of signs of chronic constrictive pericarditis

Pneumococcal Pericarditis

Dry pericarditis may result by extension of the infection from lobar consolidation of the lungs Purulent pericardial effusion is a rare complication of pneumonia, it has been seen even less frequently since the introduction of the sulfonamides and penicillin Evacuation of the pus is usually indicated Surgeons prefer the posterior approach in order to obtain adequate drainage from the lower part of the pericardial cavity Cure has been recorded when penicillin (20,000 units) was instilled into the pericardial cavity following pericardial tap, together with the use of penicillin intramuscularly and the administration of sulfadiazine. It is likely that penicillin alone in adequate doses is sufficient.

Staphylococcal Pericarditis

Staphylococcal pericarditis is rare but is seen in metastatic staphylococcal septicemia. Penicillin should be used. Large doses may be required. The addition of

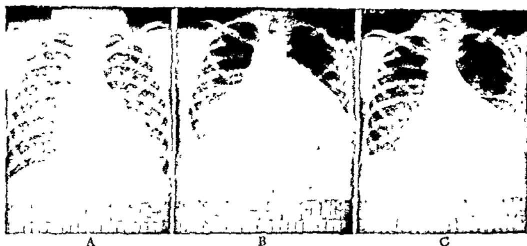


Fig 46

Changes with Pericardial Effusion in a Girl 14 Years of Age (2 Meter Roentgenograms) A, April 30, 1935, after pericardial tap, B, May 24, 1935 before, and C, May 25, 1935 after 600 cc of fluid were removed from the pericardial cavity (Stewart, H J, Crane, N F, and Deitrick, J E Recurrent pericardial effusion of unknown etiology Bull New York Acad Med 13 11, 1937.)

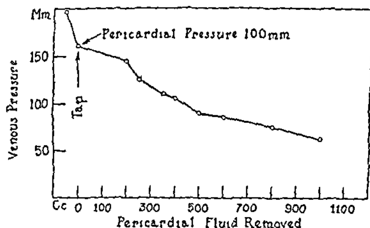


Fig. 47.

unknown etiology *Bull New York Acad Med* 13:11, 1937.)

both aureomycin and streptomycin may be necessary. Evacuation of the pus by surgical drainage may be indicated.

Streptococcal Pericarditis

Streptococcal pericarditis may be seen as a part of septicemia. It may follow an a [illegible] The treatment is similar to that of staphylococcal pericarditis: [illegible] The fluid may form very rapidly. [illegible] -tomy-cin should [illegible] tions penicillin [illegible] d be tested in order to provide adequate dosage.

Pericarditis Due to Tularemia

Acute pericarditis has been described in tularemia. The combined use of streptomycin and sulfadiazine has been found effective In the light of more recent observations streptomycin is the drug of first choice, but experience may show that aureomycin is more effective.

Acute Pericarditis Due to Amebic Infection

Acute amebic pericarditis has been described. It results from extension of amebic abscess of the liver. Drainage and appropriate antiamebic therapy should be carried out.

CHRONIC PERICARDIAL EFFUSION OF UNKNOWN ETIOLOGY

Chronic pericardial effusion may occur in the absence of evidence of a definite etiologic agent by laboratory examinations. I had occasion to observe for two and one-half years a girl, 14 years of age when first seen by us, who had suffered over a period of seven years from persistent and recurrent pericardial effusion with the typical clinical picture of recurrent tamponade. Pericardial taps were required at intervals, three years before death they became necessary every six to eight weeks. Repeated cultures of the fluid exhibited no organisms. She had no clinical evidence of infection She was stunted in growth because of the long-standing cardiac tamponade with impairment in circulatory efficiency She exhibited all the signs of cardiac tamponade: increase in venous pressure, prolongation of the circulation time, decrease in cardiac output, swelling of the eyelids, fluid in the pleural cavities, enlargement of liver, ascites, edema, tachycardia, small pulse pressure, paradoxical pulse, absent cardiac pulsations on fluoroscopy, and a large water bottle contour of the cardiac shadow (Fig 46). On removal of 1000 cc. or more of fluid from the pericardial cavity the patient improved, the venous pressure fell, the circulation time became shorter, the cardiac output increased, dyspnea became less, ascites decreased, the blood pressure increased The intrapericardial pressure was 100 mm. of pericardial fluid when the venous pressure was 150 mm. (Fig. 47). Following pericardial tap the patient was comfortable. She went to school until six to eight weeks later when reaccumulation of fluid required another pericardial tap. Mer-

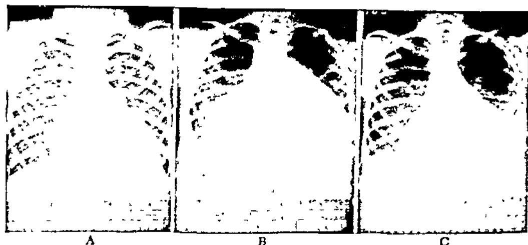


Fig 46

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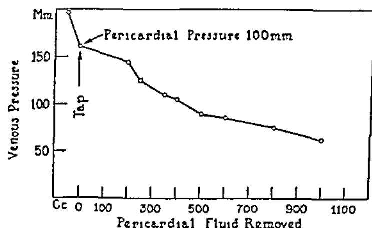


Fig 47.

Fall in Venous Pressure with Removal of Successive Amounts of Pericardial Fluid, and Intrapericardial Pressure at Insertion of the Needle before any Fluid was Withdrawn in a Girl 14 Years of Age. At this tap performed on February 27, 1936 (the thirteenth one) 1175 cc. of fluid were removed (Stewart, H. J., Crane, N F., and Deitrick, J E.. Recurrent pericardial effusion of unknown etiology. *Bull. New York Acad Med.* 13.11, 1937.)

carditis by the use of powder or iodine, or by some of the methods employed by Beck; in short, to convert the presenting syndrome of pericardial effusion into chronic constrictive pericarditis, with the notion that this complication could be remedied later by pericardiectomy. But this procedure also was abandoned, because fluid might continue to form; then, should it be loculated it would be incapable of effective evacuation by pericardial tap.

This patient suffered no ill effects from the exploratory operation; the speed of reaccumulation of fluid was not altered and pericardial taps were required at approximately the preoperative frequency. The patient managed for two years longer without any significant change in her course. She succumbed at 16½ years of age to an overwhelming attack of lobar pneumonia due to Type III pneumococci. This case history was recorded in the period before sulfonamide drugs and penicillin had been introduced. At autopsy no adequate explanation for the occurrence of chronic pericardial effusion was demonstrated. The pericardial sac, which was moderately thickened, was a large, flabby, wrinkled bag after the fluid was evacuated.

This case is cited at some length because it illustrates the problem of medical management of this patient and the measures which were considered to provide relief by various surgical procedures. Moreover, it serves as a good illustration of the purely mechanical problem of the heart carrying on as a pump when it is subjected to tamponade.

TREATMENT OF PERICARDITIS AND PERICARDIAL EFFUSION OF OTHER THAN INFECTIOUS ORIGIN

Acute Pericarditis in Myocardial Infarction

A to-and-fro pericardial friction rub occurs in approximately 10 per cent of patients with acute myocardial infarction. Pericarditis results when the area of infarction is directly under the visceral pericardium or, if the infarcted muscle is in the deeper layers of muscle at the beginning, when it extends outward and the visceral pericardium becomes roughened. Pericardial friction rubs are heard more frequently when the infarcted area is located in the anterior apical area than when the posterior base region is damaged, unless the area of infarction in the latter is very extensive. Signs of pericarditis appear a few days after myocardial infarction occurs. Sterile effusion of any significance is rare. Ice bag, sedatives, and oxygen tent may be required to alleviate the precordial pain—measures which may also be appropriate in the management of the myocardial infarction.

Pericardial Effusion in Congestive Heart Failure

Pericardial effusion occurs infrequently as a manifestation of congestive heart failure. With absorption of fluid a pericardial friction rub may appear. It requires no special treatment apart from that which is necessary because of the heart failure.

Pericardial Effusion in Nephrosis

Pericardial effusion occurring in patients suffering from nephrosis does not require special medical therapy.

curial drugs, limitation of fluid intake, and restriction of salt intake delayed the recurrence of fluid, but diuresis was not sufficient to delay its massive reaccumulation beyond two months. Measurement of cardiac output at various levels of venous pressure showed that the cardiac output decreased progressively as the venous pressure rose (Fig. 48). We were at a loss to assign a cause for the recurrent effusion.

Dr. George J. Heuer made an exploratory operation with three ideas in mind:

1. He proposed to discover whether there was obstruction by a band or by localized adhesions which might afford a mechanical background for the clinical picture

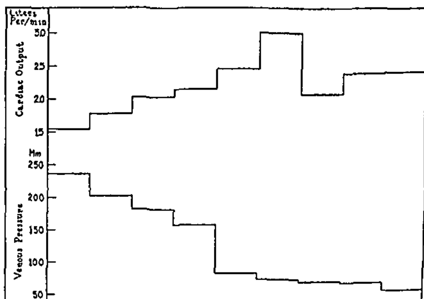


Fig 48.

[illegible] in a *Girl 14 Years* [illegible] order, disregarding [illegible] have been plotted [illegible] cardial effusion the [illegible] idies of the circula tion in pericardial effusion *Am Heart J* 16 189, 1938)

2. The notion was entertained of resecting the pericardium if the heart hung freely within the cavity. The pericardium is not essential to health, as is demonstrated by congenital absence of the pericardium and by the removal of at least a part of the pericardium in the treatment of chronic constrictive pericarditis. At operation the heart proved to be free in the pericardial cavity. Pericardiectomy was, however, abandoned for the following reasons Should fluid continue to accumulate it might spread throughout the chest cavity, its removal by paracentesis might then be impossible. Moreover, should adhesions form the fluid might become loculated and its removal by tap would be impossible or hazardous Consequently a compromise was made and the pericardium was removed from the anterior surface only.

3. Serious consideration was given to the artificial induction of obliterative peri-

Pericarditis from Other Causes

Pericarditis with hemorrhagic effusion may be due not only to tuberculosis It may arise also from rupture of a myocardial infarct or of a mycotic aneurysm, or from a dissecting aneurysm Hemorrhagic fluid may be due to metastases from malignant tumors which invade the pericardium. Such effusions have resulted from the use of anticoagulant drugs. Metastatic involvement of the pericardium may give rise to the syndrome of chronic constrictive pericarditis. If the tumor cells are radiosensitive, x-ray therapy may give temporary benefit On the other hand shrinking of the tumor tissue and replacement by scar tissue may accentuate or induce compression of the heart.

The pericardial effusion occasionally found in the presence of anemia requires no therapy, and disappears with restoration of the blood count and hemoglobin toward normal levels

TUMORS OF PERICARDIUM

Primary tumors of the pericardium are rare though metastatic involvements are common Sarcoma, carcinoma, endothelioma, leiomyoma, teratoma, and cysts of the pericardium have been reported.

Primary tumors of the pericardium may compress the heart in the region in which the tumor arises. Report has been made of a leiomyoma which encroached upon the space of the right auricle, death resulted when sudden hemorrhage into the tumor compressed the auricles Primary mesothelioma of the pericardium has been described. A malignant sarcoma of the pericardium may obliterate the pericardial cavity, completely surround the heart, leading to signs of cardiac compression or chronic constrictive pericarditis

CYSTS OF PERICARDIUM

Cysts of the pericardium occur Sometimes they can be removed surgically.

Cushing, in a summary of the literature relating to diverticula of the pericardium, has reported a case which was treated by tapping the cyst formed by the diverticulum filled with fluid. The cyst presented as a localized bulging to the right of the sternum The shadow of such a cyst may be confused with aortic aneurysm or dermoid cyst There may be increased intrapericardial pressure. Aspiration of fluid and replacement by air shows air in the pericardial cavity In about half of the cases the tumor presents to the right There is no pathologic explanation for this apparent area of weakness in the pericardium. The wall of the cyst is indistinguishable from normal pericardium It may be a congenital defect.

Pericardial Effusion in Myxedema

Some of the enlargement of the cardiac silhouette in myxedema has been attributed to pericardial effusion. Moderate amounts of fluid can be obtained on tap. The venous pressure is, however, not elevated It is unlikely that the amount of fluid sufficient to account for the total enlargement could be present without producing tamponade, unless its slow development over years allowed accommodation by the pericardium. Some of the increase in the cardiac shadow may be due to intrinsic changes in the heart muscle. The effusion is not of such proportions that it requires special treatment or removal, since it regresses with the administration of thyroid extract and with restoration of the basal metabolic rate toward normal levels

Pericarditis in Uremia

A pericardial friction rub may be heard in uremia The cause of the pericarditis is not known. No special treatment is required An ice bag and sedatives relieve pain but most commonly this complication is without symptoms even in the presence of a loud rub, which may produce a palpable friction fremitus Pericardial effusion may occur Pericarditis may be a terminal manifestation of chronic nephritis.

Pericarditis in Acute Nephritis

Acute pericarditis manifested by a typical to-and-fro friction rub may occur in acute nephritis. Ice bag and sedatives may be required for relief of pain.

Acute Pericarditis in Lupus Erythematosus

Acute pericarditis may occur in lupus erythematosus and may provide an important facet in the mosaic of symptoms which contribute to the diagnosis of this disease There may be pericardial effusion, which may form rapidly, lead to tamponade, and require removal by pericardial tap. Adhesive pericarditis may develop. This manifestation may regress with the use of ACTH.

Acute Pericarditis in Periarteritis Nodosa

Acute pericarditis may occur in periarteritis nodosa Sedatives and an ice bag to the precordium may be necessary to relieve precordial pain. This manifestation may regress with the use of ACTH

Cholesterol Pericarditis

Cholesterol pericarditis has been described in patients with xanthomatosis Treatment is symptomatic.

Leukemias, Boeck's Sarcoid, Lymphosarcoma, Hodgkin's Disease

These conditions may involve the pericardium by extension of the mediastinal lymph nodes or by seeding of leukemic areas in the heart muscle. Pericarditis results with to-and-fro friction rub. Typical electrocardiographic changes of pericardial involvement may be recorded. Pericardial effusion may follow Benefit may result from x-ray therapy if the tumor is radiosensitive.

TECHNIC OF PERICARDIAL TAP

Rationale

Pericardial tap should be done only after mature consideration. It should serve a well-defined therapeutic or diagnostic purpose, namely (1) to remove pericardial fluid because of cardiac tamponade, and (2) to be certain of the presence of fluid, to discover its characteristics, and to submit it to culture and to animal inoculation. In borderline cases angiocardiography will reveal whether the increase in size of the cardiac silhouette is due to cardiac enlargement or to fluid within the pericardial cavity.

Procedure

The patient is given an appropriate sedative, either morphine or codeine. If he is not too sick he should be propped up in bed, almost upright if possible This allows the fluid to accumulate in the lower part of the pericardial sac. When a roentgenogram can be obtained beforehand, it shows the extent of the cardiac silhouette

The procedure is carried out under sterile precautions. After infiltration of the skin and subcutaneous tissues with procaine, an 18-gauge short bevel needle is inserted *anteriorly* in the fifth rib interspace inside the outer limit of cardiac dullness and outside the point of maximum impulse if it can be felt, and within the shadow defined in the x-ray photograph The needle is directed upward and medially so that it enters the pericardial cavity parallel to the heart If the amount of fluid is estimated to be small the same procedure is carried out but it may be necessary to have the needle enter the pericardial cavity perpendicular to the heart If suction is made on the plunger of the syringe, fluid may be obtained before the point of the needle is too close to the heart to be hazardous The needle has beforehand been attached to a three-way stopcock and 50-cc. syringe. The syringe allows slow removal of the fluid Too rapid emptying of the cavity might result in acute dilatation of the heart.

If the effusion is large and the intrapericardial pressure is high, the distention of the neck veins decreases, the blood pressure and pulse pressure increase, and cyanosis fades as fluid is removed The apex impulse may become visible and, as the amount of fluid in the cavity decreases, the heart, as it beats, may strike against the needle. The patient may experience a vague sense of uneasiness as this occurs but usually does not complain of pain The hazard of pericardial tap lies not so much in puncturing the heart, which can be done without too much danger, but in puncturing or tearing a coronary vessel This accident would cause hemorrhage into the pericardial cavity, which would probably be fatal

I prefer the approach described above for pericardial tap Other clinicians prefer the *posterior approach* Under some circumstances this approach may be advised, especially if the physical signs are in the posterior chest at the angle of the left scapula In this case the needle is inserted at the angle of the left scapula

Other physicians recommend the *epigastric approach*. The needle is inserted just below the ensiform process and directed upward toward the back, and inward. Care must be exercised not to enter the peritoneal cavity Still another approach occa-

CONGENITAL ABSENCE OF PERICARDIUM

Congenital absence of the pericardium has been reported. This defect gives rise to no signs or symptoms. The heart is said to be unusually movable in the mediastinum.

PNEUMOPERICARDIUM

The presence of air and fluid in the pericardial cavity can be diagnosed on auscultation from the typical sloshing sounds as the heart beats Patients may be aware of the churning sounds X-ray photographs of the chest reveal the presence of air and fluid with a fluid level It may be of diagnostic help when pericardial fluid has been removed by tap, to put a small amount of air in the pericardial cavity and take x-ray photographs of the heart afterward. This aids in establishing the size of the heart and the presence of adhesions.

ACUTE MEDIASTINITIS

Etiology

Acute mediastinitis is serious It may result from extension of infection from the pleurae to the mediastinum. The most common cause, however, is trauma of the esophagus with extension of infection to the mediastinum. Infection is usually caused by organisms which comprise the flora of the mouth Esophageal trauma may result from swallowing a fish bone or chicken bone, or a piece of broken bottle.

Clinical Manifestations

The cardinal features are rise in temperature, substernal distress, signs of compression of the heart, increased venous pressure, increased heart rate, paradoxical pulse, fall in blood pressure, and electrocardiographic changes indicative of acute pericardial involvement. The infection progresses rapidly to the formation of an abscess in the mediastinum.

Treatment

This area does not lend itself to adequate surgical drainage, because of the many planes which are available for extension of the infection It may, however, be required Until recently many of these patients succumbed to the infection. This prognosis may now be favorably altered with the prompt use of streptomycin, penicillin and other antibiotics as indicated, and sulfadiazine in adequate amounts. When patients are treated by chemotherapy and apparent cures follow, close observation should be continued for many months after the drugs have been discontinued, for there may remain a nidus of infection which may light up again.

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sionally used is the insertion of the needle just to the right of the sternum in the fourth interspace inside the right border of dullness and inside the cardiac silhouette as shown roentgenographically.

It is my opinion that if fluid is not obtained when the physician feels reasonably certain that the pericardium has been punctured and that the needle is in the pericardial cavity, extensive exploration should not be done by pushing the needle in and out and redirecting it. Sometimes tilting the needle will suffice. It is usually safer, if the diagnosis of fluid is certain and tap is necessary, to try another location than to keep stabbing around in this area

A syringe is safer to use than a suction bottle since the flow of fluid can be more easily controlled. The 18-gauge blunt needle is satisfactory for most taps When empyema of the pericardial cavity is suspected, however, one of a larger gauge may be necessary to provide for the possibility that the pus is thick.

SUMMARY

Inflammation of the visceral and parietal layers of the pericardium may result from a variety of pathogenic organisms In other instances it may be due to viral infection, or to an infection of unknown etiology. Pericarditis may also be a clinical manifestation of a wide variety of diseases, as well as neoplastic involvement of the pericardium. In any of these the pericarditis may be dry, or it may be associated with pericardial effusion The fluid may be clear, serosanguineous, or may appear grossly bloody. In some instances pericardial effusion gives rise to compression of the heart—tamponade—and decompression by pericardial tap is required. Electrocardiograms and x-rays of the chest are useful in detecting pericardial involvement.

Treatment of acute pericarditis is symptomatic unless the offending organism is sensitive to the available antimicrobial agents Radiosensitive tumors involving the pericardium may shrink under x-ray therapy. In acute infectious pericarditis, except that due to active rheumatic infection, the possibility of chronic constrictive pericarditis following sooner or later must be kept in mind.

Acute mediastinitis is a serious disease and may be fatal unless prompt and ade- [illegible] bating the infection

[illegible] the introduction of antimicrobic agents. Tuberculous pericarditis, which until recently carried a poor prognosis, has been found to respond to streptomycin therapy in the few cases which have been reported and benefit has followed pericardiectomy carried out in the acute stage. Owing to advances in the surgical treatment of diseases of the [illegible]

of the patients are in the older age group. All observers who have had an extensive experience with this disease are agreed that the syndrome is not a manifestation of rheumatic infection.

In some instances the pericardial infection is acute and the patient is very sick In the majority of cases the infection must have been of low grade, since it gave rise to no marked symptoms and the onset could not be determined.

AGE, SEX, DURATION

The ages of the patients in our series ranged from 7 to 57 years. Three cases have been seen in the 7- to 9-year period; the remainder of them were about equally distributed in the three decades from 10 to 39 years of age, and two-thirds of the cases fell within this 30-year period. There were only a few cases in each of the two following decades. The syndrome was more frequent in males The duration of symptoms extended from a few months up to 15 years at the time the patient was first seen. Approximately one-third of the patients had suffered from their symptoms for under one year, one-third for two to three years, and one-third for four to 15 years.

EVOLUTION OF THE SYNDROME

This disease illustrates the consequences which follow interference with the mechanical workings of the heart when it is encased in a constricting fibrous membrane which acts like a vise, together with the complete recovery which is achieved when this restraining covering is adequately removed For this reason an over-all view of this disease is given so that its cure by surgical means will stand out vividly.

The following course of events is not uncommon A patient is under observation for an acute pericarditis with effusion. The causative agent will not be identified, although the fluid may be subjected to all the known culture technics During the pericardial effusion the patient has signs of cardiac tamponade: distention of peripheral veins indicating increase in venous pressure, dyspnea, enlargement of the liver, and perhaps ascites, pleural effusion, and edema Eventually the pericardial fluid is absorbed, with disappearance of the signs and symptoms Then the signs of chronic constrictive pericarditis appear, either in the course of a few months or almost immediately following the above events, with recurrence of venous distention, reappearance of enlargement of the liver, of ascites, of pleural effusion, and of edema. I have observed this sequence in several patients.

Many patients with chronic constrictive pericarditis with no history of acute pericarditis have suffered respiratory infections with pulmonary signs at some time in the past. It is not unlikely that a few of these were unrecognized instances of acute pericarditis with effusion, and the pulmonary signs resulting from compression of the lung were interpreted as lobar consolidation. I know of one instance in which this reconstruction of the history appears warranted. Furthermore, in acute respiratory infections serial electrocardiograms and x-ray photographs of the chest have sometimes revealed pericarditis with effusion which would otherwise have escaped detection. In many cases of acute pericarditis with effusion of unknown etiology, in

CHAPTER 21

Diseases of the Pericardium and Mediastinum. II. Chronic Constrictive Pericarditis

(Pick's Disease)

Chronic constrictive pericarditis is characterized by thickening of the pericardium with complete or partial obliteration of the pericardial cavity and by constriction of the heart in such a way as to interfere with its mechanical efficiency, giving rise to signs and symptoms which are like those seen in ordinary congestive heart failure. Calcification of the pericardium may occur. It is also known as Pick's disease, concretio cordis, and chronic compression of the heart.

In patients with Pick's disease there is evidence only of primary pericardial involvement, pleural effusion and ascites arising as compression of the heart occurs On the other hand in Concato's disease there is inflammation not only of the pericardium but also of the pleura and peritoneum, giving rise to fluid in these cavities.

ETIOLOGY

The etiologic agent is probably an infection, but usually the infecting agent is not detected In a certain number of cases tuberculosis is the cause, Blalock's series contains the highest percentage among those reported. This may have been because many of Blalock's patients lived in the southern part of the United States, where the incidence of tuberculosis is greater and because there was a higher proportion of Negroes. In our series of 25 patients tuberculosis was proved to be the etiologic agent in only 2 cases, in Paul, Castleman, and White's published cases the incidence of tuberculous infection was 9 in 53 patients. Andrews, Pickering, and Sellors, in England, were of the opinion that tuberculosis accounted for a large per cent of their cases. The tuberculin test is not helpful in establishing the etiology since most

PATHOLOGY

It will be recalled that the normal heart is covered with a thin layer of tissue (the visceral pericardium) and lies within the thin pericardial sac (the parietal pericardium). The two opposing pericardial surfaces are smooth and glistening, and a small amount of pericardial fluid lubricates the surfaces. In chronic constrictive pericarditis the pericardial cavity may be obliterated completely or only in certain areas. The parietal pericardium may be more involved or both may be equally affected. Thickness of the pericardium varies in different areas from a few milli-



Fig. 50

Chest of a Man 36 Years of Age When first seen this man was thought to have pericardial effusion. He was followed from the stage of effusion to absorption and then constriction, with appearance of syndrome of chronic constrictive pericarditis

A, July 24, 1935, when patient was considered still to have a moderate amount of pericardial effusion. This observation was made sixteen months before operation

B, November 11, 1936, shows the heart shadow is smaller Pericardiectomy was done on November 25

C, September 22, 1938, twenty two months after operation, shows that the heart has decreased in size after resection of the pericardium This patient was cured by operation. (Stewart, H J, Andrus, W. D, and Heuer, G J · "Chronic Constrictive Pericarditis" in Nelson's Loose Leaf Medicine New York, Thomas Nelson & Sons Vol 4, Chapter 27, p 601, 1950)

meters to nearly one centimeter. Its texture may be leathery and fibrous (Figs. 49 and 50) or there may be calcium deposits in plaques, in a branchlike network, or in a thin sheet or a bony shell which completely encases the heart (Fig. 51). The pericardial sac may be loosely attached to the visceral pericardium and thence to the heart by fibrous strands, or it may be so firmly attached that a cleavage plane cannot be demonstrated at operation. In certain patients a cleavage plane can be obtained at operation between the pericardial sac and the visceral pericardium. But this is not adequate—the visceral pericardium must also be resected A cleavage plane must be obtained between the visceral pericardium *and the heart muscle* if benefit is to result from operation. The contracting down of the thickened pericardium may implicate either the whole heart, or predominantly the left ventricle, or the right ventricle, and occasionally the great vessels.

which an adequate follow-up has been achieved, chronic constrictive pericarditis has not been detected.

In many patients the disease comes on insidiously and slowly and patients are not seen until evidence of the syndrome is unmistakable.

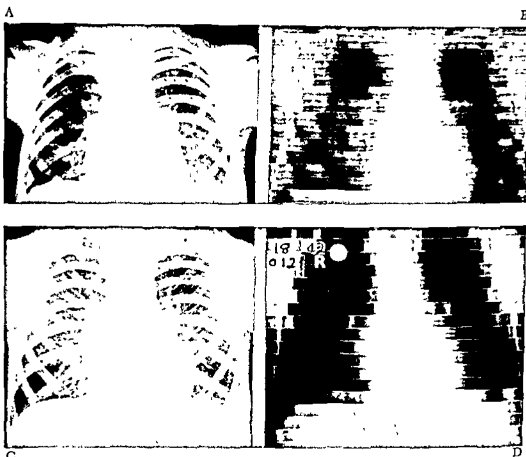


Fig. 49.

Chest of a Boy 7 Years of Age, Suffering from Chronic Constrictive Pericarditis

At some time in the course of the development of this syndrome, calcification of the pericardium may occur. I have not, however, observed its appearance clinically in patients we have followed from the stage of acute pericarditis with effusion through to the stage of constrictive pericarditis. It is probably a manifestation in cases of longer duration.

In long-standing cases the pericardium, when exposed at operation, may be pale and leathery. In patients operated earlier after the acute episode the pericardium is beefy red and vascular, so that blood oozes from the surface as it is incised or as a cleavage plane is made. In two instances this was so marked that separation of the visceral pericardium from the heart muscle could not be accomplished.

Under the microscope there is no essential difference between the calcified and the uncalcified lesions. In both types of lesions the collagenous tissue stains irregularly with the trichrome technic. If light green and xylidin ponceau are used as dyes, precalcific areas may be identified. The two instances of tuberculous pericarditis in our series were of the fibrous, diffuse type.

Adhesive pericarditis in patients with rheumatic heart disease need not be the cause of confusion with Pick's disease, because of the presence in the former of valvular disease. In adhesive pericarditis compression of the heart does not occur. Embarrassment of the heart results from the heart having to pull against the chest wall. The Brauer type of operation—removal of the ribs overlying the heart—may afford mechanical benefit (p. 233).

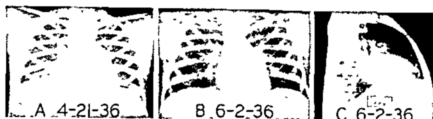
CLINICAL MANIFESTATIONS

In chronic constrictive pericarditis all the signs and symptoms of congestive heart failure may be present in varying degrees, but the more common causes of the latter disorder, such as rheumatic valvular disease, hypertension, congenital heart disease, and arteriosclerotic heart disease, cannot be demonstrated. Under these circumstances the diagnosis of chronic constrictive pericarditis should be considered.

Engorgement of the veins is one of the most prominent signs. The neck veins are full; the veins of the forehead may be distended even with the patient sitting up; infrared photographs of the body may show fullness of all the peripheral veins (Fig 52).

Varying degrees of cyanosis and dyspnea may be present, the latter even in the absence of pleural effusion. Râles at the lung bases, unilateral or bilateral pleural effusions, and thickening of the pleura may be found. The liver is enlarged Usually there is ascites In most cases there is at some time edema of the lower extremities.

The cardiac rhythm is usually regular but auricular fibrillation may prevail. The heart may be small (Figs. 49 and 51), normal, or moderately (Fig. 50) or greatly enlarged. Confirmation of the size is made later when fluoroscopy is carried out and two-meter roentgenograms of the chest are taken (Figs. 49, 50, and 51). The blood pressure is usually low, although elevated if the syndrome comes on in a patient who already has hypertension. The pulse pressure is small and paradoxical, that is to say, it *decreases* in volume with *inspiration* and *increases* in volume with *expiration*. This sign is of importance only in fitting together the whole clinical picture as it is seen in athletes, in patients with pulmonary disease, and in the presence of pericardial effusion The heart sounds may be faint or normal. Valvular murmurs are not conspicuous, but a faint systolic murmur may be heard at the apex. Broadbent's sign has not been helpful in diagnosis in our series; it is a sign of external adhesions.



Before operation

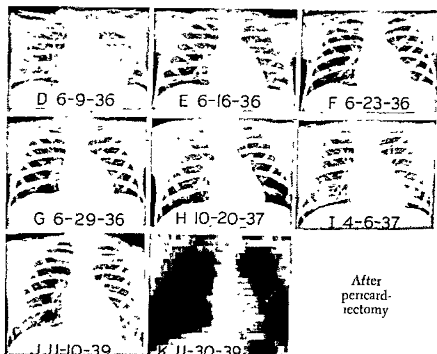


Fig 51

Chest of a Girl 15 Years of Age Suffering from Chronic Constrictive Pericarditis

A, an anteroposterior view taken April 21, 1936, about six weeks before operation, shows a relatively small heart which is pushed up by the diaphragm because of ascites

In *B*, taken June 2 just before operation, chest is clearer, heart smaller, diaphragm lower *C*, a lateral view taken the same day, shows the rim of calcification along the margin of the heart

Pericardiectomy was done on June 5, 1936 X-ray photographs *D* through *K* record changes in size and shape of heart after operation It is apparent that the heart became somewhat larger after operation and the chest remained clear.

D taken June 9, 1936 four days after operation was taken with a portable machine E was taken June 16, 1936, *F* June 23, *G* June 29, *H* October 20, *I* April 6, 1937, and *J* November 10, 1939 *K*, a kymogram taken November 30, 1939 shows good pulsations of the left cardiac border Kymograms were not taken before operation

The patient was cured by pericardiectomy and remained free of signs and symptoms without medication

Electrocardiograms of this patient are shown in Fig 53

pericardium. The aortic knob may be small and the aortic pulsations diminished, but the pulsations in the pulmonary artery region may be of good extent. Calcification may be located The heart may be fixed in the mediastinum and may not shift as the patient bends to the right and to the left side from the waist. The heart may be attached to the diaphragm and tug on it at each systole. This sign can be demonstrated when the patient takes a deep breath and holds it. Pleural fluid and thickening may be seen.

Two-meter x-ray photographs of the chest reveal the *size of the cardiac silhouette*—namely the heart together with the thickened pericardium (Figs. 49, 50, and 51) Too much emphasis should not be placed on the small heart as the size of the x-ray *shadow depends on the size of the heart before chronic constrictive pericarditis was* superimposed and upon the thickness of the pericardium—which may amount to one centimeter on each side.

Calcification occurs in approximately half the cases. It may be seen in Figure 51 Special spot films and oblique views may be used to show its extent and location Calcification may be in plaques, sheets, or a thin or thick layer encasing the heart (Figs. 51 and 56).

Roentgenkymograms show decreased motion of the margins of the heart (Fig 49); they are useful for comparison with the postoperative roentgenkymograms (Figs. 49 and 51).

Electrocardiograms in typical cases show low amplitude of the QRS complexes and T waves (Fig. 53). There is usually no axis deviation, but there may be slight right or left deviation The T waves may be low, flat, or negative and coved Normal rhythm (Fig 53) was about three times as frequent as auricular fibrillation in the cases of our series The electrical axis of the electrocardiogram may remain fixed as the patient's position is changed from lying flat to lying on the right and left side, or may shift

The ballistocardiogram may have an abnormal configuration.

The vital capacity may be normal or only slightly decreased and depends upon the presence of fluid in the pleural cavities.

The total serum proteins have been normal in most patients but may be low in those with long-standing enlargement of the liver In these patients the serum albumin fraction shows more reduction than the serum globulin The liver function may be slightly impaired as a consequence of chronic stasis.

The blood volume may be normal or increased

PATHOLOGIC PHYSIOLOGY

Before pericardiectomy the *cardiac output* per *minute and* per beat and the cardiac index—the cardiac output reduced to liters per square meter of body surface per minute—are decreased (Fig 54) The arteriovenous oxygen difference is increased and the oxygen consumption *is normal The circulation time is prolonged.*

The venous pressure is elevated (Fig. 54) This can be measured directly by inserting a needle into an antecubital vein with the arm placed at the level of the right auricle, and observing the height a column of salt solution attached *to it rises.*

When the foregoing clinical picture is seen while none of the common causes are apparent, a more extensive examination is indicated to determine the presence of chronic constrictive pericarditis. Fluoroscopic, x-ray, and electrocardiographic studies, roentgenkymograms, and observations of cardiac output, circulation time, and venous pressure may contribute to the diagnosis.

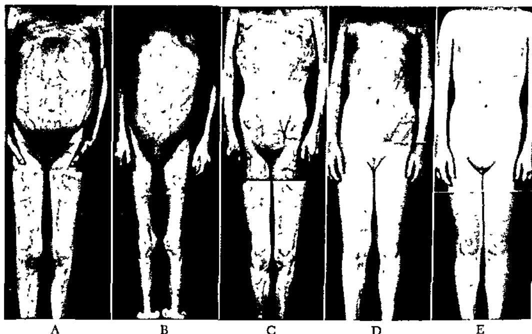


Fig 52

Infrared Photographs of a 14-Year-Old Girl Suffering from Chronic Constrictive Pericarditis, Recording Changes in the Venous Bed after Operation

A was taken on May 20, 1936 Operation was performed June 5, 1936 *B* was taken June 29, about three weeks after operation (abdomen is smaller, veins are less prominent), C on October 20 (ascites has disappeared, the veins are less prominent), *D* on April 4, 1937 (veins are less prominent, deformity of the chest due to prolonged abdominal distention with ascites has disappeared), and E on November 12, 1937, 17 months after operation (veins are no longer visible) [illegible] no longer be seen in the last [illegible] ardiectomy are apparent from [illegible] igs 51, 53, and 54).

[illegible] Watson, R F, and Wheeler, C H Measurements of the circulation before and after resection of the pericardium *J Clin Investigation* 17 581, 1938

Heuer, G J, and Stewart, H J The surgical treatment of chronic constrictive pericarditis *Surg Gynec & Obst* 68 979, 1938

Stewart, H J, and Heuer, G J *Chronic constrictive pericarditis Dynamics of the circulation* and results of surgical treatment *Arch Int Med* 63 504, 1939)

The most striking feature observed fluoroscopically is *decrease or absence of pulsations* so that the heart is said to be "quiet" or "silent." Pulsation, however, may be normal in some areas and decreased or absent in others The patient is rotated in order to visualize the pulsations on all margins. The amplitude of pulsations provides a guide to the extent and location of adhesions and thickening of the

Effect of Pericardiectomy in a Girl 15 Years of Age Suffering from Chronic Constrictive Pericarditis.

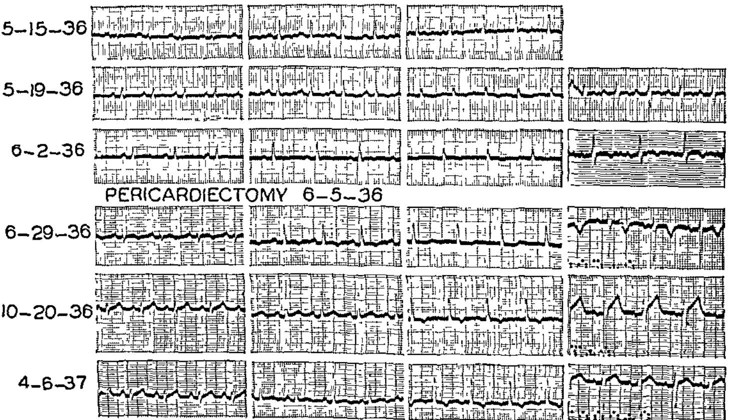
Electrocardiograms on May 15, May 19, and June 2, 1936 were taken before pericardiectomy. These show low amplitude of QRS complexes and of T waves together with negativity and coving of T waves in Leads II, III and IV.

As patient became free of ascites and fluid accumulations in preparation for operation, amplitude of QRS complexes increased and heart rate became slower

Pericardiectomy was performed June 5. Following this, venous pressure fell, cardiac output increased, circulation time became shorter, and patient spontaneously became free and remained free of fluid accumulations

Electrocardiogram taken June 29 shows T_1 is negative and coved, T_2 is more negative and coved, and amplitude of QRS in Leads II and III have increased. T_4 is more negative These changes in T waves are probably associated with pericardiectomy. In the course of time QRS complexes increased in amplitude and $T_{1, 2 \text{ and } 4}$ became upright and of good amplitude.

Electrocardiograms taken October 20 and on April 6 show these progressive changes X ray photographs of this patient are shown in Figure 51. This patient was cured by operation. See also Figures 52 and 54



LEAD I
LEAD II
LEAD III
LEAD IV
5-15-36
5-19-36
6-2-36
PERICARDIECTOMY 6-5-36
6-29-36
10-20-36
4-6-37

Fig 53.

grams increase. These physiologic observations indicate that there are two main defects in this syndrome (1) obstruction to the entrance of blood into the chambers of the heart which interferes with its filling; and (2) compromise of the contraction of the heart.

TREATMENT

Medical Measures

General Remarks

Many patients are improved by the medical regimen but most of them should be given the benefit of surgical treatment It has been found that partial resection of the pericardium—pericardiectomy—by its decompression of the heart provides cure for many patients, and marked relief for many others Pericardiectomy appeared to be indicated and has been recommended to all patients suffering from this syndrome who have been seen in our clinic

Our medical regimen is as follows·

Bed Rest

The patient is put at complete bed rest; tub bath and lavatory privileges are not allowed. I have seen no harm from bed rest in these patients; thrombophlebitis has not occurred even though the patients exhibited marked edema and varicosities of the veins of the lower extremities as manifestations of the syndrome They are encouraged to move their legs, admonished not to lie in one position for long periods but to move frequently and to take a half dozen deep breaths several times a day in order to expand the lungs

Fluid Intake

The fluid intake is limited to 1200 cc. daily I have been unable to free patients of fluid accumulations without restriction of the fluid intake.

Diet

A diet low in salt and high in protein is used. Restriction of the sodium ion, not of the chloride component, is the important factor. An attempt is made to keep the daily salt intake within 2.0 Gm. This can be achieved if Lonalac is used as a substitute for part of the protein intake The high protein diet is advantageous if the serum proteins are low In this part of the regimen fresh milk must be kept to a minimum A moderate amount of milk can account for the total salt allotment for 24 hours Moreover milk consumes too much of the fluid intake quota.

Weight Recording

The total fluid intake and total urine output are recorded daily, and the patient is weighed daily before breakfast after voiding. These two procedures allow visualization of the loss of fluid and provide an accurate guide to the effectiveness of medical therapy. Patients can be trained even in a hospital to manage their fluid intake and urine output charts.

The range in our series has been 150 to 350 mm., the normal value being 100 mm. by our technic. The venous pressure can be estimated roughly by observing the level at which veins on the dorsum of the hand collapse. Examination of the eye-grounds shows marked distention of the veins, which is to be expected with the

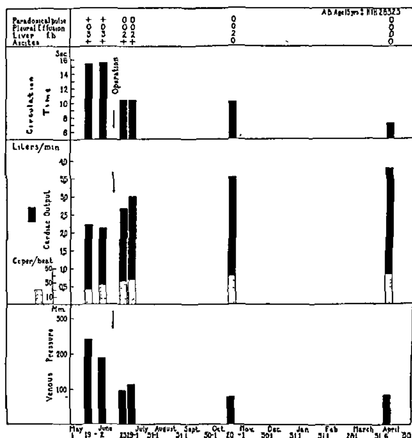


Fig 54

Data before and after Pericardiectomy Relating to Cardiac Output, Circulation Time and Venous Pressure, and Prominent Physical Signs in a 15-Year-Old Girl with Chronic Constrictive Pericarditis who Was Cured by Operation

(From Heuer, G J, and Stewart, H J The surgical treatment of chronic constrictive pericarditis. *Surg Gynec & Obst* 68 979, 1938
Stewart, H J, and Heuer, G J Chronic constrictive pericarditis Dynamics of the circulation and results of surgical treatment *Arch Int Med* 63 504, 1939
Stewart, H J, Heuer, G J, Deitrick, J E, Crane, N F, Watson, R F, and Wheeler, C H Measurements of the circulation before and after resection of the pericardium *J Clin Investigation* 17 581, 1938)

increase in venous pressure Infrared photographs may show the marked distention of all of the peripheral veins (Fig 52)

given to hold down the ventricular rate. If digitalis has not been used within two weeks, patients are digitalized throughout 24 hours in the usual way, as described in Chapters 1 and 3. Maintenance amounts are continued in order to keep the ventricular rate around 70 per minute.

Summary of Medical Treatment

[illegible]

accumulations disappear. This improvement provides a propitious setting for surgical treatment. In 2 patients I wished to see if pericardiectomy was necessary. They were gradually mobilized and permitted a gradual return to ambulatory activity, but the diuretic regimen was not altered. It was impossible to keep them ambulatory without recurrence of fluid accumulations, so they were admitted to the hospital for pericardiectomy, which was carried out after a second period of preliminary preparation. This meticulous preparation for operation appears important and has contributed to the absence of operative mortality in the New York Hospital series of these patients

Surgical Treatment

Historical Background

The uniformly unsuccessful treatment of Pick's disease by medical measures led Weill in 1895 to suggest that benefit might accrue from resection of the pericardium Delorme expressed the same opinion between 1895 and 1898 These opinions were ineffective until Rehn and Sauerbruch independently performed the operation in 1913 Schmieden in 1918 followed their lead Churchill reported the first cases operated in this country in 1929 Since then surgical treatment has been generally accepted and large series of cases have been accumulated in this country by Churchill and White, Blalock and Burwell, Heuer and Stewart, and Harrington.

Decortication of the heart by partial resection of the pericardium is the operative procedure for Pick's disease. This operation should not be confused with that described by Brauer, known as cardiolysis Brauer's procedure is undertaken to relieve the heart of excessive work in tugging against the thoracic wall when there are external and internal pericardial adhesions. It mobilizes the thoracic wall by resection of the costal cartilages and ribs to which the pericardium is adherent. Cardiolysis would of course be of no benefit in the disease we are now considering because constriction of the heart is the occasion for embarrassment of the heart. (The Brauer type operation is described in greater detail in Chapter 7, p 233)

When Is the Patient Ready for Operation?

The goal in the treatment of chronic constrictive pericarditis is to free the patient of fluid accumulations, pleural effusion, ascites, and edema by medical means if this can be attained In a few patients it may be necessary to remove pleural effusion and ascites by tap During rest in bed and the diuretic regimen, the patient's general condition improves, the state of nutrition improves, and even though he may lose fluid accumulations, he may begin to gain weight again. It may be difficult to abstain

Diuretics

MERCURIALS. In most instances one of the mercurial diuretics is indicated: mercuzanthin, salyrgan-theophylline, mercuhydrin, or thiomerin. I usually give 2.0 cc. of the drug intravenously on every third day. Mercuhydrin and mercuzanthin may be used intramuscularly and thiomerin subcutaneously. The last is the drug of choice I do not subscribe to the daily use of these drugs, even in small doses Care should be exercised during intravenous injections to protect the veins, there should be no occasion for thrombosis or hematoma if a good technic is maintained. When diuresis becomes less marked with the current mercurial preparation I change to another preparation In fact, there are cases in which I shift back and forth from one mercurial diuretic to another.

AMMONIUM CHLORIDE. To enhance the effect of the mercurial diuretics, 1 0 Gm. ammonium chloride three or four times a day may be used, in enteric-coated tablets. It does not seem to me that the enhancement of diuresis is greater when the drug is given only on the day preceding the mercurial injection. However, it is not required in most patients.

UREA On the days when the mercurial diuretic is not given, 30 cc of a 50 per cent solution of urea may be administered three times a day to increase the output of urine. Its taste is less disagreeable if the solution is kept refrigerated and is given with a little grape juice

THEOCALCIN AND AMINOPHYLLIN Although they are rarely required, theocalcin 1 0 to 1.5 Gm. three times a day or aminophyllin 0.1 Gm. three or four times a day may be useful adjuncts.

Chest and Abdominal Taps

Fluids are not withdrawn by tap from the pleural and abdominal cavities for therapeutic purposes unless they cannot be removed by diuresis. In this way the body is not deprived of the protein in these fluids If it is not possible to dissipate them by diuretics, taps are resorted to just before operation, in order to be certain that the patient is in the best state possible at the time of operation With the chest free of fluid and with ascites absent, better expansion of the lungs is achieved and the patient is relieved of much respiratory embarrassment When a chest tap has been done roentgenograms should be made before operation to be certain that air has not entered the pleural cavity.

Venesection

I do not recommend venesection even though the venous pressure is elevated. Lyons and Burwell have shown that neither this procedure nor the acute increase of the blood volume changed the cardiac output, but that the venous pressure changes ran parallel to changes in blood volume.

Digitalis

Digitalis is contraindicated in this syndrome unless auricular fibrillation or other arrhythmias arise. Since heart failure in the usual sense is not encountered, benefit from its use is not to be expected. In the patients with auricular fibrillation, it is

cavity. Streptomycin appeared to exert a favorable influence on the temperature and operation has been delayed until activity of the infection has subsided.

Blalock and Levy and more recently Holman and Willett have advocated operating early during the active acute stage for constrictive pericarditis resulting from tuberculous pericarditis and effusion, since the outcome is so uniformly fatal in most cases left to run their own course. Whether the use of streptomycin will alter the course in such patients remains to be studied Isonicotinic acid hydrazine may be effective in treating tuberculous pericarditis. Although our experience with the case just cited would seem to contradict this recommendation—early operation—the uniformly good results reported by Holman and Willett would warrant further trial.

I have recommended operation to every patient suffering from Pick's disease whom I have had occasion to observe. All patients have had the typical signs and symptoms of this syndrome in varying combinations and degrees. Improvement has been apparent in all patients we have treated medically before operation.

Care should be taken that this improvement is not allowed to go on to relapse before operation and that undue delay in surgical treatment does not give the condition a chance to become refractory to the medical regimen. This is particularly likely to happen to the diuresis if the use of mercurials is prolonged We would then be deprived of an essential part of preoperative conditioning. Operation may be expected to be a greater benefit if it is undertaken before chronic stasis in the liver induces permanent damage and before the appearance of chronic malnutrition, our experience has strengthened this view.

Anesthesia

We use intratracheal ether and oxygen Slight positive pressure can be used for reinflation of the lungs if either pleural cavity is entered, and the bronchial pathways can be kept free of secretions by aspiration. Postoperative complications attributable to anesthesia have been rare. I have not found increased irritability of the heart that could not be related to mechanical stimulation during pericardial resection. Cyclopropane is not advisable because of the tendency of this drug to induce irritability of the heart and to result in ectopic rhythms. I have found that anesthesia is effected more smoothly if the patient is propped up slightly instead of being allowed to lie flat, probably because of the high venous pressure In my opinion neither fluids by hypodermoclysis nor intravenously nor blood transfusion should be given routinely during operation. The venous pressure is already greatly increased, to increase further the volume of fluid on the venous side by infusion might promote acute dilatation of the heart as decompression of the organ proceeds and as the heart herniates out through the window in the pericardium.

Procedure

Dr. George J Heuer, Dr William D. Andrus, and Dr. Frank Glenn who have operated on all the patients in the New York Hospital series, have used the approach from the left side. The skin and muscle flap is reflected in a U-shape

from rushing too early to perform the pericardiectomy before the patient is adequately prepared for so extensive a surgical procedure. However, pericardiectomy is performed when the course is stabilized and no further improvement or gains appear likely

If chronic constrictive pericarditis has prevailed for a year or more, pericardial resection may be carried out as soon as the patient has been adequately prepared. The patient should be in the best possible state before operation is attempted.

It is in the management of the patient with acute pericarditis with effusion followed by absorption of fluid and compression of the heart that it may be difficult to decide the proper time to decorticate the heart. As fluid is absorbed or removed by tap and the patient improves, there is a reversal in all the clinical manifestations described earlier, and the once abnormal pathologic physiology is restored to or toward normal levels Then, either merging with this course or several months later when the heart is small or decreasing in size, venous engorgement recurs, the liver becomes large again, ascites and pleural effusion reappear, together with peripheral edema, and finally the picture of Pick's disease with compression of the heart is manifest as a result of the fibrotic changes in the thickened pericardium. I believe that in these cases operation should be delayed until activity of the infection has subsided, this may require many months The temperature curve, white blood cell count, and sedimentation rate are useful guides. However, in patients with calcification of the pericardium these signs may continue to be abnormal for a considerable period and should not be the occasion for delaying operation. Even after waiting many months for the activity of the acute infection to subside, the pericardium at operation may still be beefy red, vascular, and friable; a cleavage plane, however, may be secured between the heart muscle and the visceral pericardium, and an effective pericardiectomy achieved, followed by excellent recovery of the functional capacity of the heart.

On the other hand, in 2 patients with histories similar to the foregoing the time was finally considered proper for pericardial resection after observation for many months In one of these patients a cleavage plane could be developed between the pericardial sac and the visceral pericardium. The latter was greatly thickened, beefy red, and vascular. But a cleavage plane could not be found between the visceral pericardium and the heart muscle. The visceral pericardium was shaggy and blood oozed from its surface, as well as from small areas of the heart muscle which were exposed. The pericardial sac was removed from the anterior surface of the heart, but the heart remained constricted by the visceral pericardium. In short, decompression was not achieved. Further attempt to complete the pericardiectomy was abandoned. The patient recovered from this operation without incident but, as was to be expected, without improvement It had been hoped that at a later time, after the infection had subsided, resection of the visceral pericardium could be completed The patient's condition did not, however, appear favorable for a second operation. He gradually became worse and died 11 months after the first operation. From the clinical course before operation and afterward, it did not appear that operation altered the course unfavorably.

The second patient was found at operation to have a thickened pericardium with thick grumous material due to active tuberculous infection in the pericardial

cavity. Streptomycin appeared to exert a favorable influence on the temperature and operation has been delayed until activity of the infection has subsided.

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Dr George J Heuer, Dr. William D. Andrus, and Dr. Frank Glenn who have operated on all the patients in the New York Hospital series, have used the approach from the left side. The skin and muscle flap is reflected in a U-shape

incision (Fig 55). The third, fourth, fifth, and perhaps the sixth costal cartilages are resected. Some surgeons emphasize the importance of total resection of the costal cartilages and ribs in the belief that the thoracic wall over the heart should remain mobile Heuer, Glenn, and Andrus have, on the other hand, carried out subperichondrial and subperiosteal resection so that in course of time regeneration of ribs and restoration of the bony chest wall take place The sternum has not been resected to enlarge the approach, although this could be done if it appeared



Fig 55

Chest after Pericardiectomy Performed on a Girl 15 Years of Age Suffering from Chronic Constrictive Pericarditis who Was Cured by Operation (Heuer, G J, and Stewart, H J The surgical treatment of chronic constrictive pericarditis. *Surg, Gynec & Obst* 68 979, 1938)

necessary The left pleura and lung are reflected to the left If the pleura is entered, the lung can be expanded and the opening sutured If it is widely opened the edges of the pleura can be sutured to the lateral pericardial wall beyond the line of the proposed resection. More recently the trend has been to open the left pleura to obtain wider exposure A good exposure of the pericardium is made before starting the resection

The left ventricle has been liberated first in order that this cavity will be ready to receive the increased amount of blood from the right side as resection proceeds. If the right side is freed first the thin-walled right ventricle may

suffer acute dilatation following its sudden release, because of its inability to force blood through the still constricted and feebly contracting left ventricle. Some surgeons do not think this precaution is necessary.

A cleavage plane is sought over the left ventricle between the myocardium and the visceral pericardium and the small opening enlarged by blunt dissection As the opening is increased the heart muscle herniates out through it. As much of the pericardium has been removed as could be reached—to the left around the lateral margin, extending around the apex, and if possible freeing the diaphragmatic surface. The excision has then been carried to the right as far as possible over the right ventricle but has not been extended over the thin-walled right auricle. Tilting the table slightly to the left at this stage will allow the right side to fall away from the sternum and provide a wider approach. Care must be exercised not to enter the right pleura

The pericardium will have been removed in fragments, leaving a flap until the end to be used to control bleeding should the heart muscle be torn. Where there is calcification, rongeurs may be required to bite off pieces of the pericardium which have been freed from the myocardial surface. On occasion when the calcium is embedded in the myocardium, buttons of it have been left in place.

Damage to coronary arteries must be avoided In some instances when the heart bulged markedly through the window in the pericardium, incisions have been made at right angles to the edge of the remaining pericardium, giving it a saw-toothed edge and providing additional enlargement of the opening There has neither been occasion to proceed far in dissection over the thin-walled right auricle, nor to identify and to attempt to remove scar tissue from the thin-walled superior and inferior vena cava

When an adequate amount of the pericardium has been removed closure is made in successive layers. Closure is made without drainage Fibrous strands of tissue may form between the heart and the chest wall, but they have not given rise to further adhesions and recurrence of compression.

By working carefully and watching blood pressure, respirations, expansion of lungs, and the color of the patient, the surgeon has been able to resect as much of the pericardium anteriorly as the exposure would permit in our cases. We have had no occasion to terminate the operation before this objective has been attained The operative procedure has required two to three hours.

Recently White, Alexander, Churchill, and Sweet have employed cardiac catheterization to localize the site of compression of the heart Increase in pressure in the pulmonary artery indicated left auricular and ventricular compression. In such patients they have exposed the heart by a left transthoracic approach, so that adequate exposure of the left side of the heart could be secured posteriorly as well as anteriorly

Cardiac Rhythm During Operation

During pericardiectomy the surgeon and the clinician have an excellent opportunity to observe the response of the heart to mechanical stimuli. During blunt dissection of the pericardium from the myocardium and tugging on the flap of pericardium already lifted up, there may be a shower of premature contractions

or short runs of paroxysmal rapid rhythm for a few beats If the surgeon stops momentarily, the basic rhythm of normal sinus mechanism or auricular fibrillation is restored and he may safely proceed. We have not thought there was need to use procaine locally or intravenously, or quinidine. The heart appears to tolerate a tremendous amount of manipulation of its surface without developing prolonged abnormalities in its rhythm and without persistent embarrassment of its function, and with only transient effects. Nevertheless a wise surgeon respects the capacity of the heart and works carefully and gently. In many patients with normal rhythm or auricular fibrillation, there are no alterations in rhythm during pericardiectomy. On the other hand in the former, transient runs of auricular fibrillation, auricular flutter, and auricular paroxysmal tachycardia, and increase in number of auricular premature contractions (which were present before operation) have been recorded electrocardiographically during operation In patients with auricular fibrillation, ventricular premature contractions and runs of ventricular paroxysmal tachycardia have been demonstrated. Permanent reversion to normal sinus rhythm occurred during the mechanical stimulus of dissection of the pericardium in one patient who was known to have had auricular fibrillation for at least two years. This is, however, the only patient with chronic auricular fibrillation in our series exhibiting reversal to normal rhythm. Pronestyl should be available for immediate use should rhythms sensitive to it occur.

Circulatory Changes During Operation

Episodes of fall in blood pressure may occur during operation. These have not been alarming and have in no instance fallen to shock levels; nor were infusions and transfusions required, although they were available for immediate use in case of accident. These episodes may occur with each bout of premature contraction or of paroxysmal rhythms The pressure rises as the surgeon waits a few moments, and during reversal to the basic rhythm. If the pleura is entered and air enters the pleural cavity, increase in respiratory rate and fall in blood pressure may occur These are corrected with expansion of the lung and repair of the pleural tear.

As resection proceeds and the window in the pericardium is enlarged, the heart is decompressed, cardiac contractions increase, and the blood pressure and the pulse pressure both increase. It is inferred that the cardiac output increases. The engorgement of the neck veins may decrease.

Treatment Immediately After Operation and During Convalescence

We place patients routinely in an oxygen tent for several days after operation. If a tent is not available, oxygen may be given either by mask or a nasal catheter. One hundred percent oxygen is rebreathed every 15 minutes until the patient reacts

In order not to dilate the heart, which has just been released after long compression, we have not used fluids intravenously during or after operation. For the same reason we do not recommend transfusions. There have been no emergencies in our experience which have warranted their use. Slow intravenous infusions were carried out during operation on two patients but this is not recommended as a routine procedure.

Normal *saline* and 5 percent *glucose* in 1500- to 2000-cc. amounts are given by hypodermoclysis in the first 24 hours after operation It is started at the end of the operation if there have been no indications to initiate it earlier.

The patient's *position* is changed frequently to prevent pulmonary stasis and the blood pressure is taken frequently.

Morphine is given as indicated. This is added reason for changing the patient's position frequently.

We have used *sodium penicillin* G routinely for a few days after operation—25,000 to 50,000 units intramuscularly every two to three hours up to 500,000 units a day. The same objective can now be accomplished by giving 300,000 units of procaine penicillin twice a day. Before the introduction of penicillin we used sulfonamides routinely after operation, in the usual manner. Penicillin is now the antibiotic of choice, unless tuberculosis is the causative factor, in which case streptomycin would be given.

When auricular fibrillation is present *digitalis* in maintenance amounts is continued to keep the ventricular rate slow. If there is nausea, maintenance amounts of digitoxin may be given intravenously for a few days.

Hypodermoclyses are discontinued as soon as the patient can take fluids by mouth. In certain patients if nausea and vomiting do not occur, transition to oral fluid is achieved promptly, within a matter of hours; in others it may be delayed 24 to 48 hours

As soon as solid food is taken, restoration of the 2.0-Gm *salt diet* and of the 1200-cc. daily fluid intake is instituted This is usually on the third day after operation

The use of *diuretics* after operation varies Patients have been rendered free of fluid accumulations before operation If the venous engorgement has decreased with operation and complications do not arise we take these as favorable signs; observations are made several times daily for the return of râles, pleural effusion, ascites, and edema If none of these recur in the early postoperative days diuretics are not used However, if any of the foregoing signs should recur, one of the mercurial diuretics and ammonium chloride are used in the same manner as before operation. Restoration of the preoperative regimen may be necessary

When operation does not afford prompt benefit and diuretics are ineffective, *paracenteses* may again be required

Treatment of Postoperative Complications

If *pneumothorax* has occurred at operation and air still remains in the pleural cavity it is removed by means of a syringe We usually arrange for a portable x-ray of the chest immediately after operation for comparison with later films

Should fluid collect in the left and, less frequently, in the right pleural cavity, it is removed by *thoracentesis* The fluid may be clear or serosanguineous Moderate rises in temperature may occur if the fluid contains blood Fever subsides with its removal.

Atelectasis may give rise to or increase the cyanosis It may cause fall in blood pressure. Suction through a tube inserted into the trachea may remove a mucus plug. If there is chest pain which interferes with breathing and coughing *inter-*

costal nerve block with procaine may be carried out. The cough reflex is essential in order to permit the raising of sputum. If expansion of the lung is delayed and circulatory embarrassment occurs it may be necessary to bronchoscope the patient in order to remove a mucus plug.

Pneumonia is treated with penicillin. Sulfadiazine is used if penicillin is not available The fluid intake need be only slightly increased because of the fever

Should *paroxysmal auricular fibrillation* occur, the patient is digitalized in the manner which is applicable to the state of the patient (Chapter 5, p 150). If auricular fibrillation persists after digitalization, quinidine may be used (Chapter 5, p 147). I have not observed other rhythms after operation but such as occur should be treated in the appropriate manner.

Mobilization After Operation

Patients are kept at complete rest in bed for at least one month after operation in order to allow the newly released heart to gain some reserve and obviate dilatation After the first few days patients are allowed to be propped up in bed The duration of convalescence has varied from patient to patient. Patients have been free of fluid accumulations before mobilization was begun. Mobilization is accomplished gradually in a manner similar to that for patients with congestive heart failure (Chapter 1, pp 23-25). Patients first sit up, then walk, then are accorded lavatory privileges, finally tub baths If the patients have progressed to this stage they are able to take care of themselves on discharge from the hospital After discharge from the hospital they are kept on restricted or gradually increasing activity until it is apparent that cure has resulted or until the patient's capacity has been reached.

Patients who need mercurial diuretics are given the required amounts once or twice a week while in the hospital and after discharge, as indicated. Mercuzanthin, mercuhydrin, salyrgan-theophylline, and thiomerin may be used intravenously and intramuscularly, and thiomerin may be given subcutaneously One to two cubic centimeters may be given If, for instance, the patient initially requires 2 0 cc. of thiomerin subcutaneously twice a week, the diuretic is not stopped suddenly. The interval between injections is increased to once a week for a few weeks; if that goes well the interval is increased to once in ten days; if there is no reaccumulation of fluid the interval is further increased to once in two weeks. The interval is increased in this fashion until it becomes apparent that the patient can manage without this medication After a period without mercurial diuretics more liberal allowances of fluids are allowed, and then the salt restriction is lifted If at any time the patient's maximal activity and minimal medication have been reached, the program of further liberalization of activity is interrupted

Patients with chronic auricular fibrillation continue to take digitalis to keep the resting ventricular rate at approximately 70 beats per minute Restoration of normal rhythm by the use of quinidine has not been attempted in these patients

Immediate and Long-range Postoperative Course

Certain patients have enjoyed uncomplicated convalescent periods after operation, while others have experienced certain of the complications which have already

been mentioned. In some cases postoperative improvement has been rapid and neither mercurial diuretics nor other medication to mobilize fluids have been required. In the first six to eight weeks after operation all the signs of the syndrome progressively disappeared. Abnormal signs or symptoms did not recur with reinstitution of activity. Patients could be looked upon as cured These patients from this stage on were considered to be normal persons from the point of view of their activities.



Fig 56

Roentgenogram of Heart at Autopsy, Showing Extent of Calcification in a Male 29 Years of Age, who Was *Unimproved by Pericardiectomy*

Framework of calcium encircling the whole heart is apparent In upper part of photograph is seen a window which was cut in calcium shell at time of pericardiectomy From extent of calcification it is apparent that amount of decortication which was achieved was inadequate

Other patients have shown slower improvement, with gradual disappearance of all signs and symptoms of this syndrome over a period of several months. During this time they have required frequent or occasional mercurial injections In six to 12 months "cure" appeared to have taken place, residual signs and symptoms of Pick's disease could not be detected Thereafter these patients were permitted to lead normal lives

In other patients improvement extended over the first 12- to 15-month period after operation, with decreasing amounts of supportive therapy required, until finally all diuretic drugs could be discontinued. "Cure" was apparently achieved since neither signs nor symptoms of the syndrome remained.

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The velocity of blood flow usually shows changes which parallel those in venous pressure (Fig. 54). *Circulation time* falls to normal rapidly, or slowly, or may remain prolonged.

The *cardiac output* per minute and per beat and the *cardiac index* increase after operation in patients showing improvement (Fig. 54). If cure results the cardiac output attains or approaches normal levels.

Results of Operation

There is an over-all mortality of around 30 per cent. This includes those patients operated during the period of development of the operation and by surgeons relatively inexperienced in the technic of the operation. If only the larger series of experienced surgeons is analyzed the mortality rate is lower. In some instances the fatal outcome was no doubt due to the fact that the trauma of operation was too great for the patient to withstand, and in others it may have been that the operation failed to bring about the desired correction of the abnormal cardiovascular physiology.

In our clinic 24 patients have been subjected to pericardiectomy for Pick's disease since January, 1936 None of these patients has died during operation or the postoperative period. Three of the patients were unimproved after operation and died seven and one-half, 11 and 12 months later. Eleven of the patients may be classified as cured, nine as greatly improved. One patient has been operated upon too recently to evaluate the benefit which has resulted. The first patient operated in the New York Hospital series remains cured 16 years after pericardiectomy. All the cured or greatly improved patients returned to gainful employment, housework, or school. The patients listed as "cured" are relieved of all the signs and symptoms of their disease and are able to work and to lead normal lives without any restrictions and without any medications Those listed as "improved" exhibit some residual signs of the syndrome and although able to work require mercurial diuretics at varying intervals. We can therefore conclude that improvement or cure can be expected in the majority of the patients subjected to pericardiectomy; in our series it is 85 to 90 per cent

Only one of our patients exhibiting auricular fibrillation has been considered cured by pericardiectomy; he continues to take digitalis to keep the ventricular rate slow. In another patient with auricular fibrillation reversion to normal rhythm occurred during the manipulation of pericardial resection. The presence of auricular fibrillation apparently makes it unlikely that cure will be obtained by operation This unfavorable outcome is probably not due to the rhythm per se but to the underlying disease. Fibrillation may have prevailed for many years; moreover the congestive signs may have promoted the formation of auricular mural thrombi In these patients we have not yet thought it expedient to attempt conversion to normal rhythm by giving quinidine, while using anticoagulants prophylactically to prevent embolization. Although patients with long-standing disease have been cured, those in whom the course has been shorter have the more favorable outlook. With one exception the unimproved patients had suffered from the disease for many years. Still, the long duration

There are patients who have improved over a stretch of several years before a level has been reached. They have retained some degree of venous engorgement and of hepatomegaly; accumulations of fluid recurred if mercurial diuretics were not given These patients have returned to gainful occupations even though cure was not achieved. A few patients have shown no improvement after operation if the syndrome has been of long duration or decompression of the heart was not accomplished (Fig 56).

Changes Observed During and After Operation

ELECTROCARDIOGRAPHIC CHANGES. Electrocardiograms have been taken during operation in a few patients and in all of the patients at frequent intervals in the weeks after operation, then at longer intervals in succeeding years. It is surprising how slight the changes in the configuration of electrocardiograms have been, in view of the extent of the operative procedure: dissection of the pericardium from the muscle surface, mechanical stimulation of the muscle surface, and finally covering the cardiac muscle with layers of tissue in closing the chest Immediately following operation T waves may become negative and coved, or RS-T segments may become elevated or depressed (Fig. 53). For many months or years after operation the T waves and RS-T segments may continue to show minor alterations which do not follow definite patterns. The amplitude of the QRS complexes may increase after operation with cure (Fig 53) but other patients thought to be cured have not shown appreciable change. Shift in electrical axis of the heart with change in position of the body may increase after operation, indicating that the organ is more freely movable in the mediastinum The axis shift may run parallel to the motility of the heart observed on fluoroscopic examinations. Mobility of the electrical axis cannot, however, be used as a measure of improvement.

X-RAY PHOTOGRAPHS, FLUOROSCOPIC EXAMINATIONS, AND ROENTGENKYMOGRAMS. Portable x-ray photographs of the chest have been taken immediately after operation in order to record the pulmonary status at the time and to establish a base line for comparison with later films After recovery from operation and with improvement of the patient going on to cure, the heart may increase or decrease in size (Figs 49-51). We have attributed the increases in size in small cardiac shadows to dilatation of hearts after removal from the constricting membranes. Decrease in size has been thought to result from removing the thickened pericardium

Fluroscopic examination and roentgenkymograms taken after operation show that pulsations have increased in the areas which have been decorticated (Fig 49) and the hearts are more freely movable in the mediastinum. The pleural thickening which was present before operation has usually remained

VENOUS PRESSURE, CIRCULATION TIME, AND CARDIAC OUTPUT. The postoperative behavior of the venous pressure cannot be predicted. It may fall rapidly or over a period of many months to normal levels (Fig 54) or maintain a moderate elevation. Some patients who have experienced benefit from the operation have nevertheless had no reduction in venous pressure Disappearance of the marked distention of the peripheral veins after cure may be demonstrated in infrared photographs (*Fig.* 52).

should be satisfactorily prepared by medical measures beforehand. The measures used are similar to those for the treatment of congestive heart failure, with the exception that digitalis is not used unless auricular fibrillation is the prevailing cardiac rhythm Pericardiectomy has been accomplished without operative mortality in the New York Hospital series. A measure of this unusual outcome is without doubt due to the effective cooperation of surgeon and physician The great relief afforded by pericardiectomy in these cases is evidence of the contribution which surgery combined with supportive medical care has made in the treatment of this form of heart disease

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of the disease should not prevent operation if the patient can be adequately prepared for it

In a recent analysis of White's series it was stated that the results were satisfactory in 60.9 per cent.

Second Pericardiectomy

In three patients there has been gratifying improvement after operation, but gradual or sudden recurrence of symptoms has occurred. In these patients a second resection, now of the right side of the heart, has been carried out. It has been possible at this operation to identify the ridge of pericardium on the right side where the first resection had been discontinued. The procedure has been carried out in a manner comparable to the exposure of the heart from the left side. Dissection of the pericardium from the heart on the right side has been accomplished as extensively as possible There has been no occasion to free the inferior vena cava or the heart over the right auricle These patients have experienced second periods of improvement after operation with return to gainful activities, but since varying signs of the syndrome have been retained and diuretic measures have still been required, none of them has been considered cured.

SUMMARY

The syndrome of chronic constrictive pericarditis gives rise to profound changes in the mechanics of the circulation The mechanical compression of the heart, and occasionally of the great veins, is responsible for the development of the signs and symptoms of this disease. The etiologic agent in some cases is tuberculosis, in most instances it remains unknown. In all likelihood, however, the disease results from an infectious agent The clinical manifestations are similar to those seen in ordinary heart failure. The heart is unable to relax adequately in diastole to admit blood and is unable to contract effectively in systole to eject blood As a consequence the cardiac output is decreased, the blood moves at a reduced velocity, and the venous pressure rises. These manifestations and the consequences of the disease are reversible since they disappear and the functional capacity of the heart may be restored to normal following the resection of an adequate amount of the thickened, constricting pericardium.

Pericardiectomy results in cure in a large number of patients, to the extent that they may lead normal, active lives with occasional support from diuretics. Only a few patients are unimproved by operation This group comprises patients who have had the disease for many years as well as those who have suffered from acute pericarditis which has not become quiescent even after many months of observation The unfavorable course in the few who have not improved after operation cannot be construed as being hastened by operation, as death has occurred so long afterward. Although improvement occurs in patients with chronic auricular fibrillation, cure is less likely to occur than when normal rhythm prevails

Operation has been recommended for all these patients I have observed Patients

CHAPTER 22

Subacute Bacterial Endocarditis

The cure of subacute bacterial endocarditis with penicillin is one of the major contributions to therapeutics in recent years Most untreated cases terminate fatally. Occasional cures have been reported in the earlier literature but I did not see a single case in which cure was recorded before the introduction of the sulfonamides and of penicillin therapy.

ETIOLOGIC AGENTS

In subacute bacterial endocarditis bacteria lodge on the damaged endocardium, grow, and give rise to vegetations The site is most commonly on valves damaged by acquired cardiac disease but the infection may be superimposed upon any of the congenital defects of the heart. Subacute bacterial endocarditis is most commonly superimposed on rheumatic heart disease, namely mitral stenosis and insufficiency, aortic stenosis and insufficiency, and less commonly on lesions of the tricuspid valve The next most common predisposing defects are congenital malformations of the heart and blood vessels, such as patent interventricular septum, patent ductus arteriosus, bicuspid aortic valves, coarctation of the aorta, and pulmonary stenosis, to mention the most common Finally, in older individuals calcific aortic stenosis may be the preceding condition It is very rare that subacute bacterial endocarditis is superimposed upon syphilitic aortic insufficiency.

Nonhemolytic streptococci are the most common organisms causing subacute bacterial endocarditis, of these *Streptococcus viridans* (*alpha*) is by far the most frequently implicated These bacteria are usually of low virulence and are highly sensitive to penicillin On the other hand the enterococci, which are occasionally implicated, are highly resistant A preceding upper respiratory infection, acute tonsillitis, or tonsillectomy, abscesses of teeth, dental extractions,

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effective against the offending organism. The range which is considered adequate for the *in vivo* sensitivity of organisms which are generally encountered is from 50,000 units intramuscularly every two hours at the New York Hospital to 100,000 units every two hours at the Johns Hopkins Hospital.

The most frequent range of *in vitro* sensitivity of the streptococcus viridans causing subacute bacterial endocarditis is less than 0.1 unit per cubic centimeter of penicillin. Those strains requiring 0.1 to 0.5 units per cubic centimeter are considered moderately resistant, those requiring 0.5 to 10 units, very resistant; and those requiring 10 to 20 units per cubic centimeter, extremely resistant, and are fortunately rare, when subacute bacterial endocarditis is due to such resistant strains of organisms, streptomycin together with penicillin should be used (p 446). The dosage should be sufficient to keep the serum level of penicillin between four and five times the amount required for *in vitro* inhibition of the patient's organisms, but higher levels may be necessary to achieve cure in some patients

Although penicillin is still expensive, subacute bacterial endocarditis carries such a high mortality that there should be no compromise in giving adequate doses It should not be a question of giving the smallest effective dose, but of curing the greatest number of patients The dosage schedule varies among investigators working on this problem, and is constantly being revised A schedule of 50,000 units of sodium penicillin G intramuscularly every two hours for a total dosage of 600,000 units a day will be adequate to cover the range of sensitivity of the usual organisms The present schedule at the New York Hospital calls for this dosage for six weeks

On the other hand Tumulty and Harvey give 100,000 units of penicillin every two hours intramuscularly, and more if it appears necessary They aim to keep the blood level at five times the sensitivity level of the organism The penicillin can be increased, if need be, by daily increments to as much as 20,000,000 units until a satisfactory result is achieved They advise using the clinical course as the best guide to the amount of penicillin to administer return of temperature and pulse toward normal, gain in weight, absence of sweating, absence of embolic phenomena, improvement of the patient, and increase in hemoglobin and in red blood cell count They continue to give penicillin for at least two months after all evidence of infection has subsided

Blood cultures should be taken two to three times weekly during treatment with penicillin, then weekly for two to four weeks, and finally at monthly intervals Blood cultures should be taken more frequently if symptoms appear suggesting recurrence of infection, or if the patient suffers from an upper respiratory infection

Route of Administration

In most instances adequate blood levels of penicillin can be maintained by the intramuscular route When the responsible organism is resistant and it is essential to administer large quantities of the drug, the administration by continuous intramuscular or intravenous drip may be effective. It is probably more effective to increase the intake of penicillin than to attempt to raise the blood

otitis media, and childbirth may be the events which allowed the entrance of organisms into the blood stream. Almost every organism known to infect man has at one time or another caused endocarditis.

CLINICAL MANIFESTATIONS

The characteristics of the disease are the remittent fever, lassitude, café au lait color, petechial hemorrhages, anemia, embolic phenomena, changing murmurs, clubbing of fingers, splenic enlargement, and red blood cells in urine. In the presence of the signs and symptoms described above, the diagnosis is confirmed by recovery of the organism from the blood stream.

TREATMENT

If the clinical evidence of subacute bacterial endocarditis is convincing, therapy with penicillin in adequate doses should be instituted in large enough amounts to be effective against the common range of sensitivity. Most studies have emphasized the importance of early and adequate therapy before extensive damage has been done. Several blood cultures a day should be taken for several days After the organism is recovered *in vitro*, sensitivity can be estimated and appropriate changes made in the drug and in its dosage. Even should an organism not be recovered in serial blood cultures, if the clinical course is that of subacute bacterial endocarditis, the patient should have a therapeutic trial with penicillin It is well to have both aerobic and anaerobic cultures made. The number of colonies per cubic centimeter of blood gives an idea of the magnitude of the infection.

General Measures

The patient should be at complete rest in bed. Fluids may be allowed as desired if heart failure is not present Although the sodium chloride intake need not be limited if there is no evidence of heart failure, account should still be kept of the sodium intake, when sodium penicillin is used, especially if the drug is given intravenously or intramuscularly in salt solution. A high calorie diet should be given. The patient should be encouraged to eat liberally Mild cathartics will probably insure a daily bowel movement. Symptoms are treated as they arise, and appropriate therapy is instituted for any complications which may occur.

Penicillin

Dosage

Sodium, potassium, and calcium penicillin are available. When large quantities of penicillin are given, the salt which is selected may become of importance. Sodium penicillin G serves for most purposes

There is no general agreement on the amount of penicillin to use or on the duration of treatment. However, it stands to reason that penicillin should be used in sufficiently large amounts to produce a blood level which will be

Hematuria and albuminuria subside promptly. The sedimentation rate may fall to normal, but it may remain elevated even in patients who are apparently "cured." Embolic phenomena may occur even in patients who are adequately treated. The day-to-day improvement in the early stages of therapy is very dramatic, indeed, patients improve so rapidly that it may be difficult to enforce the continued complete rest which is necessary.

When to Mobilize the Patient

Patients should be at complete bed rest during treatment. Reports of the finding at autopsy of focal myocarditis in fatal untreated cases give additional reason for insisting on bed rest The patient should engage in only limited activity for several weeks after antibiotic treatment has been discontinued An adequate interval should be allowed as a precaution against heart failure and the hazard of rupture of a valve A longer period of rest is indicated if the patient has a greatly diminished cardiac reserve. Mobilization should be carried out gradually, just as in patients who have had congestive heart failure, in order not to strain the damaged heart.

Effect of Penicillin on Healing

With the healing of subacute bacterial endocarditis, marked changes occur in the valves and in congenital defects. Scarring deformity results which induces a mechanical hazard leading to decrease in the functional capacity of the heart Diverse stages of healing have been described in the vegetations on the heart valves of patients who have come to autopsy at different stages of treatment with penicillin With healing, the vegetations in the early stages are masses of granulation and hyalinized connective tissue which become organized and are finally converted into dense connective tissue, with areas of calcification, covered over with endothelium The completely healed valve is thick and scarred. The deformity of the valve—occurring with relative suddenness over a period of days to weeks in a valve which is already scarred—is adequate reason for the appearance of heart failure in some patients as the subacute bacterial endocarditis is apparently being cured or is cured.

Moore studied more than 100 cases of subacute bacterial endocarditis which came to autopsy after treatment with penicillin He found that healing was promoted by penicillin but that the basic principles of healing were not altered The processes which he identified were (1) The exposed surface of the vegetations became covered with fibrous tissue; (2) bacteria were phagocytosed, (3) the bacterial colonies underwent calcification, (4) the central core of the vegetations became hyalinized and calcified, (5) the spaces and clefts of the vegetations became lined with endothelium, and (6) when healing was accompanied by excessive calcification, calcific stenosis of the valve resulted

Treatment of Complications During Penicillin Therapy

CONGESTIVE HEART FAILURE Congestive heart failure may be present as a part of the increased burden on the heart caused by the infection The heart may fail suddenly with rupture of a valve during therapy. The heart sounds and murmurs

level by decreasing the excretion through the selective action of certain drugs on the kidneys.

Procaine penicillin is an insoluble salt which maintains an effective plasma concentration of the drug with a minimal number of intramuscular injections. It is suspended in water or in oil. It is possible that two or three injections daily of large amounts of procaine penicillin will be effective in the treatment of subacute bacterial endocarditis. The sensitivity of the organism will determine whether effective blood levels can be maintained by this form of penicillin. A sufficient number of cases have not been treated with the procaine penicillin to provide the basis for estimating its effectiveness.

Measures to Elevate Plasma Concentrations of Penicillin

Certain substances have been used to inhibit the renal tubular excretion of penicillin in order to raise the level of the antibiotic in the blood Diodrast, para-aminohippuric acid, and benzoic acid have been used. It is necessary to give them intravenously.

Carinamide may be given by mouth. The effective dose varies from patient to patient As much as 24 Gm. a day may be required. Maintenance of a large volume of alkaline urine may prevent crystalluria. The drug should not be used in patients with decreased renal function. It is probably better to increase the amount of penicillin, although carinamide might find use occasionally when the organisms are extremely resistant and require as much as 10 to 20 units per cubic centimeter *in vitro* to inhibit their growth. Infections with many of these resistant organisms can be treated with streptomycin and penicillin instead of with enormous doses of penicillin.

How Long Should Patients Be Treated with Penicillin?

There is no uniformity of opinion on how long penicillin therapy should be maintained. The present regimen at the New York Hospital in the usual case requires the intramuscular injection of penicillin every two hours for six weeks. Certain investigators recommend that the drug be given for five weeks; others continue it for one month after cure has been attained. Tumulty and Harvey recommend the continuance of penicillin for two months after all evidence of infection has subsided In view of the seriousness of the disease and the additional damage which results when it recurs, it is better to err on the side of prolonging treatment The emergence of drug-resistant organisms during treatment occurs only rarely.

Course of Disease During Treatment with Adequate Doses of Penicillin

There is striking improvement in the patient's condition. Blood cultures become sterile in one to two days, rarely as long as four to five days. The temperature and pulse rate subside to normal in four to five days The patient looks better and feels better The appetite improves. Gain in weight occurs and proceeds over several weeks Sweating disappears. The white blood cell count falls rapidly to normal. The hemoglobin and red blood cell count increase gradually and are normal within a few weeks, and the patient's color becomes normal.

examination, by visualization of the chambers of the heart if the signs are atypical and there is a question of additional lesions, and by temporary closure of the ductus at the time of operation to be certain that additional congenital defects are not present which contraindicate closure. Evidence of vegetations in the left side of the heart would be a contraindication to this operation Gross advocates section of the patent ductus and closure of the two ends rather than simple ligation, even in patients with subacute bacterial endocarditis.

After recovery from subacute bacterial endocarditis following the use of antimicrobial therapy, the congenital defect remains with all the resultant complications. It is unlikely that the cure of subacute bacterial endocarditis by penicillin would induce changes in the ductus which would make later ligation of the ductus more difficult or contraindicated. Nevertheless ample time—perhaps three months—should be allowed after cure of the endocarditis for the inflammation to subside before operation is attempted. Ambulatory antimicrobial therapy is continued during this time.

End Results of Penicillin Treatment

With adequate treatment around 75 to 80 per cent of the patients with early subacute bacterial endocarditis can be cured and remain bacteria-free. When the disease is due to a strain of streptococcus viridans which is highly sensitive to penicillin, cure can be reasonably expected in all cases. Frequently additional organic defects are added by the infection For instance, signs of aortic insufficiency may appear in a patient with calcific aortic stenosis. In other patients healing with fibrosis, calcification, and shortening of tendinae superimposes additional deformities of the valve which alter adversely the functional capacity of the heart Occasionally rupture of a valve may occur. The early diagnosis and inauguration of treatment make it likely that healing will occur with minimal additional deformity

Because of these alterations during the healing process it may happen that a patient whose clinical course with respect to the subacute bacterial endocarditis is satisfactory suddenly develops congestive heart failure or experiences an exacerbation of heart failure which was already present. On the other hand a patient may have been cured of subacute bacterial endocarditis, sustained mobilization completed without incident, and reached a satisfactory level of activity before congestive heart failure comes on

It is my impression that patients suffering from subacute bacterial endocarditis on the background of a patent interventricular septal defect have less alteration of functional capacity after cure with penicillin than do those with mitral and aortic lesions. The former defect probably does not lead to a great deal of deformity which can alter the dynamics of the blood flow.

Penicillin and Sulfonamides

For subacute bacterial endocarditis due to gram-negative organisms, penicillin together with the sulfonamides may be effective; the combination of the two drugs has been used effectively when the organism was *Hemophilus para influenzae*. Streptomycin is the drug of choice at the present time, however, when this organism is implicated

should be carefully followed, and the sudden appearance of signs of aortic insufficiency with a musical murmur and collapsing pulse and other appropriate signs should suggest the diagnosis of rupture of the aortic valve. Myocardial infarction may result from rupture of a mycotic aneurysm of a coronary artery or from a coronary embolism, and lead to heart failure. Cardiac decompensation may be due to active rheumatic myocarditis. The heart may fail because of decrease in its functional capacity with deformity which the valves sustain during healing. Finally, heart failure may result from too vigorous application of intravenous fluids, especially if the sodium component is more than can be managed Heart failure is treated by all the measures which are usually employed: digitalis, low salt diet, restricted fluid intake, mercurial diuretics, and other drugs as they are indicated

EMBOLIC PHENOMENA. Although embolic phenomena occur most frequently in patients who are inadequately treated, they may occur at any time during adequate therapy or even during the succeeding three to four weeks after discontinuance of therapy without necessarily indicating recurrence of the infection. There is no evidence that heparin prevents embolic phenomena; moreover hemorrhages have resulted from its use Most investigators agree that neither heparin nor dicumarol should be used When embolization occurs, arteries to the spleen, kidneys, brain, mesentery, extremities, and heart may be involved. These accidents are met by appropriate means which depend on the organ affected.

PERSISTENT BACTERIEMIA. Failure to sterilize the blood stream results either because inadequate amounts of penicillin are given or because of unusually high resistance of the organism Increasing the amount of penicillin may be effective. On the other hand, the organism may not be susceptible to penicillin, and other antimicrobial agents must be added or substituted (see p. 446).

ELEVATION OF BLOOD UREA NITROGEN. The blood urea nitrogen may become elevated and remain so This may result from decrease in renal function associated with the endocarditis or, in certain instances, to renal infarction

RECURRENCE OF FEVER After the fall in temperature to normal with the institution of penicillin therapy, the temperature may rise without recurrence of bacteriemia and with continued improvement of the patient. Occasionally the fever may be due to penicillin and the temperature will return to normal when penicillin is discontinued. Rise in temperature need not be the occasion for stopping penicillin before the course of the drug is completed In some instances persistence of fever may be due to the breakdown of infarcts

SKIN REACTIONS. In the manner in which penicillin is given in subacute bacterial endocarditis, sensitivity with skin manifestations and angioneurotic edema are infrequent.

Penicillin in the Presence of Patent Ductus Arteriosus

Subacute bacterial endocarditis grafted on a patent ductus arteriosus should be treated with penicillin in the usual manner. If sterilization of the blood stream does not occur promptly, ligation of the patent ductus should then be carried out. Ligation, in Touroff's experience, usually frees the blood stream of organisms I think, however, that the usual regimen of penicillin should be established in addition. Before the patent ductus is ligated attempts should be made by physical

in vitro as well as *in vivo* is that the streptomycin eliminates those bacteria which have survived exposure to penicillin but are partially inhibited by it.

Four out of five patients who completed an adequate course of combined therapy were cured A fifth patient died after a second course of treatment was instituted for possible relapse, even though the infection was apparently controlled.

The same authors have reported the cure of chronic recurrent nonhemolytic streptococcic endocarditis treated concurrently with penicillin and dihydrostreptomycin. The patient received 500,000 units of sodium penicillin G every two hours intramuscularly and 0 5 Gm of dihydrostreptomycin every six hours intramuscularly for 42 days. The same regimen carried out for two weeks has been effective in treating bacterial endocarditis due to penicillin-sensitive *Streptococcus viridans*.

Terramycin

Terramycin has been used in the treatment of a few patients with subacute bacterial endocarditis but it has not yet been determined whether its long-range effectiveness compares favorably with penicillin This drug is cheaper to produce than aureomycin and streptomycin and can be given orally or intravenously. The oral dose is 4 to 5 Gm a day in divided amounts, the intravenous dose is one-fifth the oral. In retarding the growth of organisms terramycin is in the same range as aureomycin and chloramphenicol It may cause diarrhea after several days' use but this is not severe enough to require that the drug be discontinued There may be loss of appetite and occasionally nausea and vomiting, but less than with aureomycin.

The place of aureomycin and chloramphenicol in the treatment of subacute bacterial endocarditis has not yet been defined but appears to be very limited. There is one report of the successful use of aureomycin in the treatment of subacute bacterial endocarditis due to penicillin-resistant organisms.

RECURRENCE OF SUBACUTE BACTERIAL ENDOCARDITIS

"Cured" patients should have routine examinations at frequent intervals to detect the clinical recurrence of subacute bacterial endocarditis Moreover periodic blood cultures should be made to detect the recurrence of bacteriemia If relapse occurs the patient should be put back to bed and another course of penicillin therapy should be instituted There is no reason to believe that the *in vitro* sensitivity of the organism to penicillin will be decreased with the relapse and patients have been found to respond favorably again to penicillin in adequate amounts. The recurrence of the disease may, however, result in further valvular damage. Naturally adequate therapy in the first course will lessen the likelihood of relapses Recurrence after many months is probably a new infection and not a relapse.

Prevention of Recurrences

Infected teeth while in the presence of subacute bacterial endocarditis should be removed toward the end of the course of penicillin therapy or after recovery has occurred Penicillin should be continued for an adequate period afterward. Whenever extraction of teeth or any oral manipulation is undertaken, the administration of large doses of penicillin (500,000 units) 24 hours before, on the day of the

Streptomycin

Streptomycin should be used when subacute bacterial endocarditis is due to penicillin-resistant or to "relatively" penicillin-resistant enterococci and staphylococci, as well as when it is due to gram-negative organisms, which are not sensitive to penicillin. The organisms of the influenza group *Hemophilus influenzae* and *Hemophilus para influenzae* are sensitive to streptomycin Dihydrostreptomycin in the same dosage is less toxic than streptomycin Streptomycin, given in such a small amount as 0 5 Gm. (500,000 units) in 24 hours, in divided doses every two hours intramuscularly for 73 days, has resulted in cure of subacute bacterial endocarditis due to organisms of the influenza group. Daily amounts of up to 2.0 Gm. intramuscularly, divided into no more than four doses, for three to four weeks at least, however, should be adequate in most instances requiring the use of this antibiotic.

The sensitivity of the offending organism to streptomycin should be estimated When allergy to streptomycin appears, benadryl and pyribenzamine may be given so that the use of streptomycin may be continued. The vestibular disturbance may be annoying. The urine should be watched for albumin, which might indicate the onset of nephrosis.

Streptomycin Combined with Penicillin

Robbins and Tompsett have recently reported on the combined use of streptomycin and penicillin in the treatment of enterococcal endocarditis and bacteremia. The organisms of the enterococcus subdivision of the genus *Streptococcus* are highly resistant to penicillin. The two most frequently encountered organisms of this group in cardiac disease are *Streptococcus fecalis* and the *Streptococcus zymogenes*. For the majority of the strains the minimal inhibitory concentration of penicillin is 3.0 to 6 0 units per cubic centimeter, in contrast to the range of the *Streptococcus viridans* group of 0 02 to 0.3 units per cubic centimeter and of group A hemolytic streptococci of 0 02 units of penicillin per cubic centimeter or less According to these authors males are more apt to be infected with this group of organisms following surgical operations on the genitourinary system, especially the prostate, among females infections are more frequently related to abortions or pregnancy. Obviously, then, most male patients affected are over 45 and most female patients are in the childbearing age

The regimen these authors recommend is the concurrent administration of 500,000 units of crystalline penicillin intramuscularly every two hours and of 0 5 Gm. of streptomycin or dihydrostreptomycin intramuscularly four times daily. The total dosage is therefore 6,000,000 units of penicillin and 2.0 Gm. of streptomycin or dihydrostreptomycin a day. The regimen is carried out for a period of 28 to 42 days whenever possible. Patients who exhibit sensitivity to streptomycin may sometimes receive the dihydro- compound without reaction.

Robbins and Tompsett point out that although the organisms might not be very sensitive to either of these two antibiotics alone, the additive effects of the two may be adequate to sterilize the blood stream and achieve cure. A possible explanation for the summative action of penicillin and streptomycin on the enterococci

tal defect. Occasionally it occurs in a patient whose heart was thought to be normal.

In most instances adequate amounts of penicillin intramuscularly will be effective. The primary infection should be rigorously treated. For instance, the intrathecal use of penicillin is indicated in pneumococcal meningitis. In gonococcal endocarditis, sulfadiazine may be used together with penicillin in the hope that all mutant strains will be eliminated by one or the other. In brucellosis, the combined use of streptomycin and sulfadiazine has been used in the past but aureomycin is now the drug of choice.

SUMMARY

The cure of subacute bacterial endocarditis by the use of antibiotics is one of the therapeutic triumphs of modern medicine. In most instances penicillin alone in adequate doses is effective; in others streptomycin alone; in others the simultaneous administration of both penicillin and streptomycin; and in others still the use of sulfadiazine may be combined with these antibiotics. The place of the newer antibiotics—aureomycin, chloramphenicol, and terramycin—remains to be defined. For optimal results with the least damage to the patient's heart, early treatment with adequate amounts of the antibiotic should be carried out. It must be kept in mind that the patient still has the underlying heart disease upon which the subacute bacterial endocarditis has been grafted, and that the anatomic defect may have been made worse by the scarring which occurs as healing of the subacute bacterial endocarditis proceeds. It should be the cause of satisfaction that a disease formerly incurable is now subject to cure in 75 to 80 per cent of all the cases and in 100 per cent of the cases in which the organism is highly sensitive to penicillin. Patients with rheumatic and congenital heart disease can now be spared what was formerly one of the most tragic complications of those diseases

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extraction, and for two to four days afterward is advised. The successful use of oral aureomycin in the following dosages has been reported: 2.0 Gm. daily in divided doses on the day before the dental extraction, on the same day, and on the day after; the last dose before operation should be given not earlier than three hours before extraction. Single extractions are preferred to multiple ones. Care of respiratory infections should be emphasized. Patients with rheumatic heart disease and congenital heart disease should be given penicillin prophylactically before obstetric, urologic, gynecologic, and surgical procedures

SUBACUTE BACTERIAL ENDOCARDITIS DURING PREGNANCY

When subacute bacterial endocarditis is encountered during pregnancy it is treated vigorously according to the plan formulated for other patients Special concern is given to the state of compensation. At the time of delivery the same factors are taken into consideration as in any other patient with heart disease. Special weight is given to the possibility that mechanical damage might have occurred during treatment and to the possibility of the precipitation of heart failure on this basis alone This is of particular importance because of the strain of pregnancy and of delivery.

Davis and Wortmann report the case of a patient treated for subacute bacterial endocarditis with penicillin at the time of delivery of a living baby by cesarean section It was found that adequate levels of penicillin were attained at the time of delivery in maternal blood, in cord blood, and in the amniotic fluid

STREPTOCOCCUS VIRIDANS SEPTICEMIA IN ARTERIOVENOUS FISTULA

Streptococcus viridans septicemia with vegetations localized on an acquired arteriovenous aneurysm of the external iliac artery and vein was described by Hamman and Rienhoff in 1935. Cure was accomplished by excision of the aneurysm Nowadays penicillin would be used as well as the surgical correction of the defect Diagnosis of this condition would require differentiation from subacute bacterial endocarditis

Cutler and Wolf have reported an acquired arteriovenous aneurysm of the femoral artery and vein complicated by subacute bacterial endocarditis of the aortic valve, and by bacterial endarteritis of the fistula due to *Streptococcus viridans*. They called attention to four other cases in the literature

ACUTE BACTERIAL ENDOCARDITIS

Acute bacterial endocarditis may develop during the course of any septicemia or bacteriemia in pneumococcic and gonococcic infections, in meningitis due to the meningococcus; in *Staphylococcus albus* infections, usually with metastatic abscesses, or in streptococcus hemolytic infections such as an acute osteomyelitis, and in brucellosis Usually it is superimposed on a previously damaged valve or congeni-

CHAPTER 23

Neurocirculatory Asthenia

(Effort Syndrome, Da Costa's Syndrome)

DEFINITIONS, SYMPTOMS

Wood has defined neurocirculatory asthenia as a group of symptoms which limit the subject's capacity for effort and by a number of signs arising from disturbance of the autonomic nervous system not due to organic disease The common symptoms are breathlessness, palpitation, fatigue, left thoracic pain, and dizziness The common signs are functional disturbance of the respiratory, vasomotor, muscular, and sudomotor systems. Wood thinks the syndrome might be more appropriately called an "anxiety neurosis with effort intolerance." Signs and symptoms of cardiac neurosis are frequently present in patients who also have symptoms and signs of organic disease of the heart.

The syndrome was described by DaCosta in 1871 as "irritable heart of soldiers" and it is sometimes known by his name In World War I Lewis originated the term "effort syndrome" Oppenheimer and Levine and others designated it as "neurocirculatory asthenia," the term which has come into common use

This syndrome assumes special importance in time of war It was a major cause of disability in World War I. In World War II, owing to careful screening, few of these subjects were inducted into the armed forces; in fact, there was difficulty in discovering enough subjects suffering from the syndrome for special study during the last war Many sufferers manage fairly well in civilian life until some unusual stress occurs, but are unable to face the strain and uncertainties of war The best policy in wartime would be to use these individuals if necessary in some noncombative service, although some of the subjects in Wood's series who were less severely ill recovered sufficiently to return to combat service.

Effort syndrome occurs in men, women, and children Its recognition is important on three accounts. (1) So that the symptoms which these patients suffer do

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manifestation may be tremor. The family history may reveal a high incidence of nervous disorders.

The symptoms may be confused with those of active rheumatic carditis, hyperthyroidism, early pulmonary tuberculosis, and, less commonly, angina pectoris when it occurs in the appropriate age group. Since neurocirculatory asthenia may occur in patients with organic heart disease, symptoms due to the former must be differentiated from those due to the latter.

The mechanism of the somatic manifestations is not known. Experiments set up in attempts to discover the cause for the signs have not been very rewarding. The manifestations appear to be set off by a central stimulus which is emotional and is frequently fear.

Cardiac Signs

The heart is slightly smaller than in subjects without neurocirculatory asthenia. But since the body build of these subjects is smaller than average, in relation to the body size the heart is of normal proportion The electrocardiogram is usually normal but may show instability of the T waves. Some authors point out that T_1 and T_2 may be flattened and occasionally may show inversion or be diphasic, others stress the instability of the T waves in Leads II and III. There may be a faint systolic murmur at the apex

The diagnosis of this syndrome may be difficult. There are no really trustworthy tests Friedman has devised a hyperventilation test The breath-holding test may be useful at other times; deceleration time of the heart after exercise may have diagnostic significance on other occasions

TREATMENT

Sufficient examination should be made to allow the physician to tell the patient firmly and with conviction that he has no evidence of organic heart disease. The label "nervous heart" should be avoided. In the description of the patient's complaints the settings in which the symptoms occur should be recorded An evaluation of the patient's attitude toward his symptoms should be made

Frequently, modified psychiatric care of the patient can be undertaken by the physician or cardiologist, especially if he is interested in the psychosomatic phases of medicine When the manifestations are more severe the attention of a trained psychiatrist may be necessary Ample time should be allowed so that the patient is not rushed and the physician does not convey the impression of haste Overuse of alcohol, tobacco, and coffee is to be avoided Adequate rest is advised By discussion with the patient and by allowing free talk some insight may be gained by the patient into his symptoms, this may help him to rid himself of signs which he has misinterpreted If the emotional symptoms are due to real fears the patient must be encouraged to overcome them or adjust to their presence and learn to live with them If the recurring stimuli are too much for him, he might be removed from the environment before the symptoms become a habit, especially during the time that he is gaining some insight The patient should be urged to engage in activities

not lead to a diagnosis of organic disease with a resultant secondary chain of symptoms, (2) so that proper understanding of the symptoms may lead to appropriate therapy with gain of insight and either cure or alleviation of symptoms; (3) so that subjects can learn to live with their symptoms, should the pattern be firmly established

Lewis stressed the response of these subjects to exercise The normal response to extreme exertion is breathlessness and fatigue Sufferers from neurocirculatory asthenia, however, complain of palpitation, pain, and dizziness; breathlessness is less frequently encountered. Aside from this abnormal response to exercise these patients have symptoms on other occasions, provoked by emotion. There is sudden weakness especially in the legs, with a sense of prostration, trembling, faintness, and syncope Many of the manifestations are like those of panic, fear, and anxiety Because they occur at rest as well as on exertion, Friedman suggests that the hypothalamus may be of prime concern in the pathogenesis of many if not all of the somatic manifestations of neurocirculatory asthenia, as the mediating but not necessarily the initiating source

PHYSIOLOGIC CHANGES TO STRESS-PRODUCING LIFE SITUATIONS

Wolf and Wolff define cardiac neurosis—a term which includes neurocirculatory asthenia—as "a group of signs and symptoms occurring in a patient as a result of disordered function of the cardiovascular and respiratory systems in response to stress-producing life situations and associated with specific emotions."

Elevation of the pulse rate is a common accompaniment of fever, anxiety, and anger Exercise carried out in the presence of emotion may give rise to a greater elevation of pulse rate than during a stress-free period and may induce a prolonged increase of cardiac output Abnormal cardiac rhythms—premature contractions, paroxysmal auricular fibrillation—may occur during stress A common response to life stress is rise in blood pressure The hyperventilation which occurs during stress may be accompanied by giddiness and weakness or fatigue

In the *hyperventilation syndrome* spontaneous attacks of hyperventilation, associated with anxiety with rapid shallow breathing, result in faintness, dizziness, palpitation, and sweating. Tetany may result from expiration of carbon dioxide

CLINICAL MANIFESTATIONS

The number of signs is roughly proportional to the severity of the case. The general manifestations are the anxious facies and nervousness The cardiovascular signs are cold hands, flushing, rapid heart rate, overactive heart, slow retardation of the heart after exercise, and elevation of the blood pressure. Inasmuch as the cardiovascular system is especially susceptible to psychic disturbances, this system is frequently the effector organ and a large number of the manifestations are referred to it. The respiratory manifestations are frequent sighing, hyperpnea, and tachypnea. The sudomotor signs are sweating of the palms and axillae A skeletal and muscular

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commensurate with his capabilities rather than to strive for goals which are beyond his attainment

Since effort plays an important role in the production of symptoms, attempts have been made to condition these subjects to greater amounts of exercise. Such a measure probably has no effect on the basic syndrome but it may serve the useful purpose of providing occupational therapy and reducing the opportunities for introspection

In the treatment of the *hyperventilation syndrome* breathing a 5 per cent carbon dioxide–95 per cent oxygen mixture may break up the cycle. Rebreathing in a paper bag may provide a concentration of carbon dioxide which is effective. Psychotherapy may yield an understanding of the underlying cause and provide permanent relief

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Traumatic coronary thrombosis has been reported in young individuals as well as in those in the older age group whose hearts have been weakened by arteriosclerotic changes. Since this accident is followed by changes like those from myocardial contusion it is not always possible to distinguish the two types of injury Patients suffering vessel damage are more likely to have anginal pain.

Rupture of aortic valve may occur as a result of trauma. The appearance of systolic and diastolic murmurs over the aortic area with other signs of aortic insufficiency and the early appearance of heart failure are the salient features. Failure would be appropriately treated. Rupture or linear tear of the aorta or dissecting aneurysm of the aorta may follow trauma A nonpenetrating blow to the maternal abdomen has resulted in cardiac injury to the fetus and its death In these traumatic accidents to valves and aorta, pre-existing disease of the aorta or valve may sometimes be demonstrated by careful microscopic examination, which would account for the tear occurring under stress

Treatment

Following cardiac trauma without hemorrhage the patient should have complete bed rest until healing has occurred Morphine or other sedatives may be required for pain Oxygen may be beneficial The treatment is the same as for a patient with myocardial infarction Heart failure may occur and should be treated in the appropriate manner. If supraventricular paroxysmal tachycardia or auricular fibrillation occurs, digitalis is indicated It is not uncommon for patients to have precordial distress as well as a poor response to exercise for a long time after recovery.

STAB AND GUNSHOT WOUNDS

Cardiac trauma of the penetrating type, from stab and gunshot wounds, is common These accidents damage both the pericardium and the heart. The cavities of the heart may be entered A coronary vessel may be damaged alone or with the myocardium When hemorrhage occurs tamponade of the heart may ensue or blood may escape into the pleural cavities

The appropriate signs of cardiac tamponade would be increase in venous pressure as shown by distention of neck veins, rapid heart rate, and falling arterial blood pressure with decreasing and paradoxical pulse pressure Changes in the dynamics of the circulation with cardiac tamponade due to stab wound of the heart or of the great vessels within the pericardium do not differ from those found in tamponade due to pericardial effusion. In both cases there is decrease in cardiac output and cardiac index, and increase in arteriovenous oxygen difference With the relief of tamponade these measurements of the circulation return to or toward normal levels (Stewart).

Treatment

General Measures

Warren, Brannon, Stead, and Merrill, by the method of right heart catheterization, have confirmed these earlier findings of Stewart and his associates, and have added data on tamponade following stab wound of the heart. They found that

CHAPTER 24

Cardiac Trauma

Trauma to the heart may result on the one hand *from nonpenetrating injuries,* wounds, or contusions and on the other, from penetrating injuries such as stab wounds and bullet wounds. The problem of foreign bodies in the heart forms another aspect of this field.

Many times the injuries are multiple, that is, to the pericardium, to the heart, and to great vessels, as well as to the chest and lungs.

CONTUSIONS

One of the common causes of contusion of the heart is compression of the chest between the steering wheel of an automobile and the vertebral column The same type of injury may arise from a kick in the sternal region by a horse The damage *may be greater if the impact occurs at the moment of cardiac diastole when the* cavities of the heart are full of blood, this will give rise to rupture of the heart If slow seeping of blood into the pericardial cavity with gradual appearance of tamponade with rise in venous pressure occurs there may be opportunity for exploration in an attempt to close the tear or to try to seal the leak with a patch of fascia or of pericardium. There may be damage to the myocardium without rupture; on exposure the heart muscle appears bruised. The electrocardiogram shows changes in QRS complexes or RS-T segments. Bundle branch block or partial auriculoventricular block may occur The electrocardiogram may go through serial changes like those seen in myocardial infarction. There may be leukocytosis and increase in sedimentation rate; a pericardial friction rub may be heard, and the electrocardiograms may show changes appropriate to pericarditis These changes may be used as guides to treatment and to duration of complete bed rest. If the damaged area of the myocardium is extensive, softening may occur with rupture of the heart This may occur at any time in the first month. Healing may take place but weakness of the wall will result in a ventricular aneurysm

Penicillin should be used promptly together with other antibiotics if they appear indicated. Because of the ready availability of penicillin, control of infection is more easily accomplished. Oxygen by tent, mask, or nasal catheter should be used as long as necessary. Patients should be kept in bed for several weeks, and then mobilized gradually.

Patients who recover following repair of cardiac wounds suffer little or no physical handicap afterward.

When emergency operation is necessary great ingenuity on the part of the surgeon may be required in order to carry out the best procedure under the most sterile emergency conditions Care should be exercised in the use of solutions to wash out the pericardial cavity. One instance of pericarditis with polyserositis has been recorded after the use of a surgical solution of chlorinated soda to irrigate the pericardial sac.

Because the mortality may be as great as 50 per cent in patients who arrive at a hospital because of cardiac wounds and are operated upon, Blalock thinks that cardiac tamponade resulting from wounds of the heart may not invariably require operation He thinks that pericardial tap may be done; if blood reaccumulates rapidly, however, exposure and suture of the heart are indicated. If more than one paracentesis is required he recommends that 15 minutes be allowed between them to encourage closure of the wound If it is thought that an auricle rather than a ventricle has been injured, operation may be more safely deferred In contrast to Blalock's view, Nelson is of the opinion that exploration should be carried out in every instance of penetrating thoracic wound in which it cannot be said positively that a cardiac wound does not exist.

TRAUMA OF THE PERICARDIUM

Traumatic rupture of the pericardium may result from compression of the thorax, from a blow to the chest, from the chest being run over by an automobile, and from laceration by fractured ribs. It occurs more frequently on the left side than on the right. Antemortem diagnosis of this single lesion is rarely possible. All the signs of acute dry pericarditis may appear

Stab wounds of the chest may penetrate the pericardium yet not damage the heart muscle. A pneumopericardium may result from a gunshot wound without damage to the heart itself, and may not require operation

Hemothorax may occur if the heart is damaged If rupture of the pericardium is suspected, it is best to open the thorax and suture the pericardial edge. Should closure not be carried out, sclerosis and narrowing of the pericardial opening later has led to constriction of the pulmonary artery resulting in death due to strangulation of the heart

Absorption of hemopericardium without any operative intervention and followed by complete recovery has been reported

When the pericardium is ruptured and the heart also damaged, more profuse hemorrhage may occur than might be the case if the pericardial opening is small and tamponade can to some extent restrict the loss of blood.

raising the venous pressure, by means of increasing the blood volume with the rapid intravenous infusion of human albumin solution, caused some improvement. Improvement is accomplished only if the additional increase in venous pressure either results in further stretching of the pericardial sac or forces some of the blood out of the pericardial sac Aspiration of the pericardium relieves the pericardial tamponade in some patients if it can be done before a clot forms. When there is evidence of internal hemorrhage into the thorax, an exploratory operation is indicated A point of differential diagnosis between the effects of loss of blood and cardiac tamponade would be the following With blood loss alone there should be no rise in venous pressure, a rise in venous pressure would therefore provide evidence of tamponade *Shock out of proportion to the apparent blood loss is further evidence of tamponade.* The blood pressure should be carefully watched. Prompt exploratory operation is indicated in either case If a splashing sound is heard on auscultation the presence of air together with blood or fluid may be diagnosed

Surgical Measures

Prompt suture of the heart muscle may be life-saving A severed coronary vessel may be ligated In suturing the heart muscle, coronary vessels should be spared if possible It may be necessary to place a traction suture in the apex of the heart to aid in steadying the heart motion during the repair Some surgeons, however, do not approve of this measure If the cardiac wound is not immediately apparent Nelson recommends the infiltration of the vagus nerve with 1 per cent procaine before extensive manipulation of the heart is attempted The rationale of this precaution is the observation that traction of the heart or bronchus is likely to be followed by bradycardia or asystole. The pericardium is closed without drainage. The electrocardiogram subsequently goes through changes like those seen in myocardial infarction following coronary thrombosis, upon which may be superimposed alterations due to pericarditis

It may be advisable to remove blood, by a pericardial tap if possible, in order to reduce the intrapericardial pressure and relieve the cardiac compression; a transfusion may be started at the same time

Morphine should be used to control pain, care being exercised not to depress the respiratory center *Sometimes a patient may be unconscious and an anesthetic is not* required for an exploratory operation. On other occasions local anesthesia may be adequate In other instances a general anesthetic is required. Nitrous oxide, cyclopropane, and ethylene-ether have been recommended, whatever is used, oxygen and positive pressure provide control over expansion of the lungs. Some surgeons use a lateral exposure, others a midsternal approach.

Whole blood and glucose solution should be used to control shock and replace fluids. In one patient *with massive continuous hemorrhage into the pleural cavity* from a severed coronary artery, autotransfusion of the blood removed from the pleural cavity was successfully carried out after filtering through several layers of gauze. Autotransfusion may be kept in mind for the occasions when blood is not readily available for transfusion, although this emergency procedure will rarely be necessary.

Penicillin should be used promptly together with other antibiotics if they appear indicated. Because of the ready availability of penicillin, control of infection is more easily accomplished. Oxygen by tent, mask, or nasal catheter should be used as long as necessary. Patients should be kept in bed for several weeks, and then mobilized gradually.

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FOREIGN BODIES IN THE HEART AND PERICARDIUM

Bullets, shrapnel, needles—venepuncture needle as well as darning needle—are some of the foreign bodies which have been encountered. Not all foreign bodies in the heart and pericardium need be removed. However, it is dangerous to allow sharp foreign bodies to remain within the heart cavities as they may penetrate later, and if within the right heart may move out into the pulmonary circuit and cause pulmonary embolism and infarction. Foreign bodies buried in the heart muscle do not cause death or shorten life. It is safe to remove foreign bodies from the pericardium and large ones should be removed.

Foreign bodies may travel for surprising distances. The literature records a breaking off of a venepuncture needle in the antecubital vein, its entry into the venous circulation and its progression to the heart and through the heart wall into the thorax. The patient was unaware of this migration and did not suffer any complaints

WOUNDS OF GREAT VESSELS NEAR THE HEART

Because of the rapid loss of blood involved, wounds of the great vessels are usually quickly fatal unless the wound is *intrapericardial*. In the latter case the pericardial sac may to some extent limit the loss of blood. Sometimes, however, closure of the defect with recovery may be successfully effected. For example, recovery has been reported following an intrapericardial stab wound of the superior vena cava In this instance, although the pericardium had been entered from a wound in the right chest anteriorly tamponade resulted from the escape of blood from the opening in the superior vena cava The low blood pressure and circulatory failure which prevailed were out of proportion not only to the amount of blood which had apparently escaped from the vascular tree but also to the amount of blood that could be demonstrated in the right chest Recovery followed suture of the superior vena cava

Recovery from a stab wound of the *pulmonary* vein has been recorded following exposure and ligation of a three-quarter-inch laceration in the superior pulmonary vein, where the vein passes from the lung into the right auricle In this instance there was massive hemorrhage into the pleural cavity amounting to approximately two liters.

Blalock has reported the successful suture of a wound of the ascending aorta resulting from a stab wound from an ice-pick. Operation was carried out under nitrous oxide and oxygen anesthesia. Successful repair of the aorta damaged by gunshot wounds has been reported Restoration of the lumen may be accomplished by suture of the aorta. Restorations of continuity of blood vessels by suitable grafts is receiving special attention.

Survival after injury of blood vessels is more likely if some of the following factors obtain: (1) If the wound is small and a clot forms during the period of hemorrhagic shock; (2) if the surrounding tissues and the blood serve as a tamponade, (3) if the formation of an arteriovenous fistula returns the blood to the circulation.

CARDIAC ARRHYTHMIAS FOLLOWING CARDIAC TRAUMA

Auricular fibrillation is one of the most common cardiac irregularities recorded after chest injuries which damage the heart. An example may be cited. One of our postoperative chronic constrictive pericarditis patients suffered the onset of auricular fibrillation after his chest had been compressed between two trucks. This accident occurred several years after operation at a time when the patient was doing well. While there had been regeneration of the ribs after operation the precordium still lacked rigidity. The onset of auricular fibrillation precipitated heart failure at a time when the patient was in a state of compensation without medication. Rest in bed, slowing of the ventricular rate with digitalis, and the regimen commonly used in treating heart failure resulted in restoration of compensation without the administration of mercurial diuretics Attempts to restore normal rhythm were thought inadvisable.

When *auricular flutter* or any of the tachycardias occur they are treated as in other patients with these rhythms

Heart block following trauma is usually transient but on occasion it is permanent It may be incomplete or complete. Transient and permanent bundle branch block have been recorded. If these are the only manifestations of cardiac injury from trauma, rest in bed is indicated until no further T wave and RS-T segmental changes occur and until the patient's symptoms and signs have disappeared or have become stationary.

Premature contractions from any part of the heart muscle may occur after trauma They are treated in the appropriate manner if symptoms are attributed to them

It is reasonable to infer that sudden death after injury to the chest or nonpenetrating wound of the heart may be due to *ventricular fibrillation* in those instances in which postmorten has not shown any cardiac damage.

SUMMARY

Most of the situations arising from trauma of the heart and neighboring vessels come within the province of surgeons, and require skillful surgery applied with great promptness if the patients are to survive the loss of blood which is a common accompaniment. The experience with this branch of surgery during the war has not yet been fully placed in the literature. Nevertheless the war experience as well as that of those surgeons who see traumatic surgery in general hospitals indicates that skill and prompt treatment may be life-saving. Treatment implies not only the application of surgery but also the combating of shock and loss of blood by intravenous fluids and by replacement of blood Finally, the new antibiotics are valuable allies in the prevention and treatment of wound infections which formerly were prone to follow these accidents should patients' lives have been spared from the immediate effects of the trauma

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CHAPTER 25

Carotid Sinus Syndrome

ETIOLOGY

The carotid sinus is the bulb at the bifurcation of the common carotid artery, covered with an extensive plexus of nerves. The nerve endings are sensitive to stretch—that is, to changes in the intrasinal pressure—and to chemical changes Four nerves contribute to the innervation of the carotid sinus and carotid body: the glossopharyngeal, the vagus, the cervical sympathetic, and the hypoglossal The glossopharyngeal nerve (ninth) and its branch, the carotid sinus nerve, transmit the afferent impulse of the carotid sinus reflex induced by pressure on the carotid sinus.

The carotid sinus syndrome is due to hypersensitivity of one or both carotid sinuses to changes in intrasinal pressure Carotid sinus hypersensitivity may result in syncope The attacks may occur without warning or they may be preceded by dizziness, blurring of vision, numbness and tingling in the extremities, and weakness, with syncope there are convulsive movements. The subject may fall, there may be hyperpnea Prominent features may include varying intensity of slowing of the heart up to asystole, and varying degrees of fall in blood pressure to the point at which it is not obtainable The attacks are followed by prompt recovery and may be transient and momentary or last several minutes. They are usually precipitated by turning the head, or by compression of the neck either when the head is bent forward or by a tight collar. Attacks occur when the subject is standing or sitting The syndrome is found more commonly in the older age group who have hypertension and arteriosclerosis It may be associated with a tumor of the carotid body or with tumors or inflammation about the carotid bulb Carotid sinus syndrome may appear after a head injury. Digitalis may increase the sensitivity of the carotid sinus.

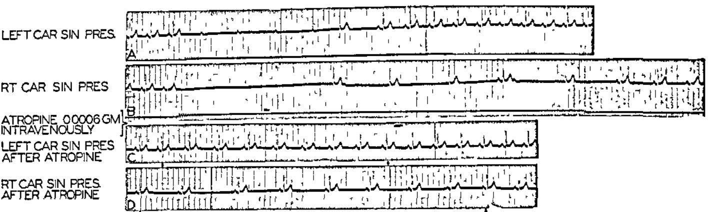


FIG 57

Electrocardiograms Relating to a Man 71 Years of Age who Complained of Attacks of Syncope

Lead II is recorded in all instances In this and the following figures the signal at the bottom of the record indicates when pressure was applied and when released A was taken during pressure over the left carotid sinus. Auricles continued to beat under the direction of the sinus node, since P waves were seen There was complete auriculoventricular dissociation with blocking of the P waves for four cycles and the ventricles were quiescent until there was ventricular escape followed by return of normal sinus rhythm with release of pressure. Fall of blood pressure and dizziness occurred

B was taken during right carotid sinus pressure This caused asystole for six seconds followed by ventricular escape, then prompt return to normal rhythm on release of pressure There was a fall in blood pressure and complete syncope.

C shows the effect of left carotid sinus pressure and *D* the effect of right carotid sinus pressure after 0.0006 Gm atropine intravenously At the height of the atropine effect, pressure on the left carotid sinus induced very slight slowing of the sinus rate with slight fall in blood pressure Pressure on the right carotid sinus induced sinus bradycardia with slight fall in blood pressure. Syncope did not occur In C and *D* arrows indicate the onset and offset of pressure (Ray, B S, and Stewart, H J Role of the glossopharyngeal nerve in the carotid sinus reflex in man Relief of carotid sinus syndrome by intracranial section of the glossopharyngeal nerve *Surgery* 22:411, 1948)

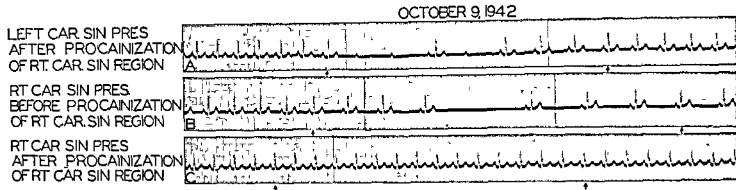


Fig. 58.

Data Relating to Patient Shown in Fig 57.

A, effect of pressure on the left carotid sinus (unanesthetized) after procainization of the right carotid sinus region. It was the same as on previous occasions (Fig 57, A) Procainization resulted in slight rise in blood pressure and slight increase in heart rate. *B*, electrocardiogram taken during pressure on the right carotid sinus before procainization of this region which showed it still to be sensitive *C*, during pressure on the right carotid sinus after its procainization. Change in heart rate and blood pressure did not occur and the patient experienced no symptoms In this figure arrows indicate the beginning and end of pressure (Ray, B. S, and Stewart, H J.: Role of the glossopharyngeal nerve in the carotid sinus reflex in man. Relief of carotid sinus syndrome by intracranial section of the glossopharyngeal nerve. Surgery, 22 411, 1948)

DIAGNOSIS

The diagnosis is made from the history in which the circumstances under which syncope occurs are defined, and by reproduction of the spontaneous attacks by pressure over the sensitive carotid sinus (Fig 57). Sometimes both carotid sinuses are hypersensitive, usually one is more sensitive than the other. Carotid sinus syncope may require differentiation from syncope associated with glossopharyngeal tic (Chapter 26) and from fainting or syncope during attacks of coughing—so-called laryngeal epilepsy or tussive syncope In the latter the heart continues beating and a radial pulse can be felt, observations which permit its differentiation from carotid sinus syndrome of the vagal type.

Weiss's investigations revealed three mechanisms or possible causes of the syncope:

1. The "vagal type" (the most common variety), in which syncope is a consequence of fall in blood pressure caused by cardiac asystole, with resulting cerebral anoxemia,

2. The "depressor type," in which the cerebral anoxemia has been caused by a fall in blood pressure without change in heart rate,

3 The "cerebral type," in which syncope occurs without any change in heart rate or blood pressure I have not seen patients exhibiting the "depressor" and "cerebral" types.

At the height of its effect (vagal release of the heart rate together with dryness of the mouth and dilatation of the pupil) atropine intravenously abolishes the effects of carotid sinus pressure, that is to say, it abolishes cardiac asystole, fall in blood pressure, and syncope (Fig. 57) Procainization of the sensitive carotid sinus abolishes the same manifestations (Fig. 58) By procainization it is possible to distinguish between syncope due to hypersensitivity of a carotid sinus and syncope due to cerebral anoxemia which may be attributed to occlusion of the carotid artery occurring during pressure over the carotid sinus Local anesthesia of the carotid sinus region results in the Horner's syndrome. small pupil, ptosis of lid, and lo[illegible] sweating of the face.

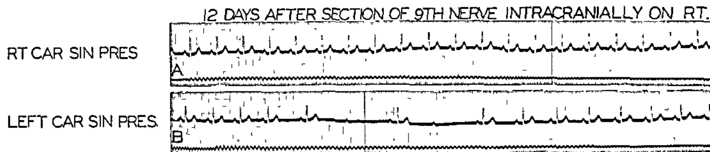


Fig 59

Data Relating to Patient Shown in Fig. 57

A, effect of pressure over the right carotid sinus after section of the right ninth nerve intracranially Immediately following operation and during the six and one half years since operation, pressure over the right carotid sinus (on the side of the nerve section) has failed to cause any alteration in cardiac rate, blood pressure, respirations, or state of consciousness *B*, effect of pressure over the left carotid sinus at this time Sensitivity of the left carotid sinus has remained unaltered from its preoperative state (Fig 57, A). In the five years since operation there have been a few mild attacks of faintness which are believed due to the hypersensitivity of the left sinus but the attacks have not been of sufficient degree to require section of the other glossopharyngeal nerve (Ray, B S, and Stewart, H J.: Role of the glossopharyngeal nerve in the carotid sinus reflex in man Relief of carotid sinus syndrome by intracranial section of the glosso-pharyngeal nerve, *Surgery*, 22 411, 1948)

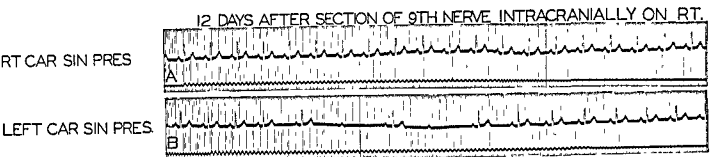


Fig. 59

Data Relating to Patient Shown in Fig 57.

A, effect of pressure over the right carotid sinus after section of the right ninth nerve intracranially. Immediately following operation and during the six and one half years since operation, pressure over the right carotid sinus (on the side of the nerve section) has failed to cause any alteration in cardiac rate, blood pressure, respirations, or state of consciousness. B, effect of pressure over the left carotid sinus at this time Sensitivity of the left carotid sinus has remained unaltered from its preoperative state (Fig. 57, A) In the five years since operation there have been a few mild attacks of faintness which are believed due to the hypersensitivity of the left sinus but the attacks have not been of sufficient degree to require section of the other glossopharyngeal nerve (Ray, B. S, and Stewart, H. J.: Role of the glossopharyngeal nerve in the carotid sinus reflex in man Relief of carotid sinus syndrome by intracranial section of the glosso pharyngeal nerve *Surgery*, 22 411, 1948)

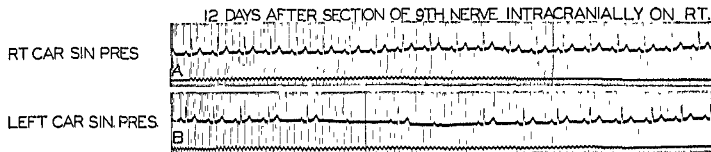


Fig 59

Data Relating to Patient Shown in Fig. 57

A, effect of pressure over the right carotid sinus after section of the right ninth nerve intracranially. Immediately following operation and during the six and one half years since operation, pressure over the right carotid sinus (on the side of the nerve section) has failed to cause any alteration in cardiac rate, blood pressure, respirations, or state of consciousness. B, effect of pressure over the left carotid sinus at this time. Sensitivity of the left carotid sinus has remained unaltered from its preoperative state (Fig 57, A). In the five years since operation there have been a few mild attacks of faintness which are believed due to the hypersensitivity of the left sinus but the attacks have not been of sufficient degree to require section of the other glossopharyngeal nerve. (Ray, B S., and Stewart, H. J.: Role of the glossopharyngeal nerve in the carotid sinus reflex in man Relief of carotid sinus syndrome by intracranial section of the glosso pharyngeal nerve. Surgery, 22.411, 1948)

Adrenalin prevents the asystole which is expected from pressure over a hypersensitive carotid sinus by stimulating a new center of impulse formation in the ventricles, which may lead to idioventricular rhythm. Adrenalin given intravenously induces the prefibrillatory state.

Ephedrine 20 to 30 mg. three times a day may also be effective, but it is not advisable to prescribe this drug over a long time for patients in the age group susceptible to coronary artery disease.

With the exception of phenobarbital, these medical measures all have side effects which limit their usefulness when given over a long period of time.

Surgical Measures

As a result of our experience we have recommended surgical treatment to all patients whose attacks of syncope were demonstrated unequivocally to be due to hypersensitivity of the carotid sinus. We have not had occasion to see aged patients who were not suitable for operation.

Two surgical procedures are effective Denervation of the hypersensitive carotid sinus by stripping the nerve plexus from the carotid bulb (both carotid sinuses may be stripped) and section of the ninth nerve intracranially.

Denervation of the hypersensitive carotid sinus has abolished the attacks and hypersensitivity. It is carried out under ether or local anesthesia This procedure has, however, some drawbacks First, the sensitivity of the carotid sinus may not be abolished by the general anesthesia, consequently the manipulation required to dissect the plexus free may precipitate prolonged asystole and fall in blood pressure The carotid vessels may be sclerotic and friable, and difficulty in carrying out the denervation may be encountered Finally there is the great capacity of this nerve tissue to regenerate in spite of wide denervation and removal of the tissue After denervation there is a transient rise in blood pressure If both carotid sinuses are hypersensitive the other carotid sinus may be denervated a few days later

A more satisfactory operation is that of *intracranial division of the ninth (glossopharyngeal) nerve* on the hypersensitive side. This can also be done under ether or local anesthesia. Suboccipital craniotomy is performed on the hypersensitive side The cerebellar hemisphere is uncovered and retracted medially to explore the region of the jugular foramen The glossopharyngeal nerve is isolated from the adjacent vagus nerve and is divided This procedure permanently abolishes the effects of pressure on the homolateral carotid sinus (Fig 59), and does not have the drawback of possible regeneration or the hazard of damage to the carotid vessel Glossopharyngeal interruption is especially applicable to cases of hypersensitivity in which local conditions do not permit dissection: cervical neoplasms, aneurysms, tubercular nodes, irradiation scars, and carotid body tumors There is rise in blood pressure after division of the nerve, with fall to the preoperative levels approximately 12 hours later. Convalescence has been uneventful and patients have remained free of attacks. There have been no untoward effects after division of the ninth nerve. Ray is of the opinion that section of both ninth nerves intracranially can be carried out if both carotid sinuses are hypersensitive, a suitable interval being allowed between the two operations.

SUMMARY

In a few patients phenobarbital may be effective in preventing attacks of syncope due to hypersensitivity of the carotid sinus. It is the only drug which is recommended for use over long periods of time For patients whose attacks occur under circumstances which may result in serious accidents and harm to themselves and to others, surgical treatment is indicated. The most effective treatment in our experience is intracranial section of the ninth nerve. Surgical denervation of the carotid sinus is the procedure of second choice.

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CHAPTER 26

Glossopharyngeal Neuralgia

(Tic Douloureux Associated with Cardiac Arrest)

ETIOLOGY

Glossopharyngeal neuralgia or glossopharyngeal *tic douloureux* is a syndrome characterized by stabbing paroxysmal pain in the tongue, pharynx, neck, angle of jaw, or ear and may be accompanied by fainting The syncope is due to cardiac arrest. The afferent pathway of the carotid sinus reflex through the glossopharyngeal nerve provides a mechanism for simultaneous neuralgia and excessive stimuli to the sinus reflex. There may be a history of preceding tonsillar inflammation In other patients the syndrome may result from herpes zoster of the ninth nerve.

CLINICAL MANIFESTATIONS

Attacks may be infrequent or may occur every few minutes during waking hours Each attack may be a series of lightning-like stabs continuing for five to forty-five seconds, subsiding suddenly only to start again a few minutes later. The pain may be of intense piercing quality, beginning on one side at the base of the tongue, spreading to the neck behind the angle of the jaw, and then deep into the ear With fleeting stabs there may be slowing of the heart With more intense and longer paroxysms there may be asystole for several seconds, followed by bradycardia and fall in systolic blood pressure to 25 to 30 mm. Hg during the pain (Fig 60) (Ray and Stewart) In the most severe attacks with cardiac arrest and fall in blood pressure there may be pallor, loss of visual fixation, confusion, or complete syncope. Recovery from syncope is simultaneous with the return of normal cardiac rate and rhythm, and with cessation of the pain. Attacks may be precipitated by swallowing and talking. This pain is not to be confused with the dull pain, so-called carotodynia, experienced by some patients with hypersensitive carotid sinuses and marked arteriosclerotic changes of the arterial walls.

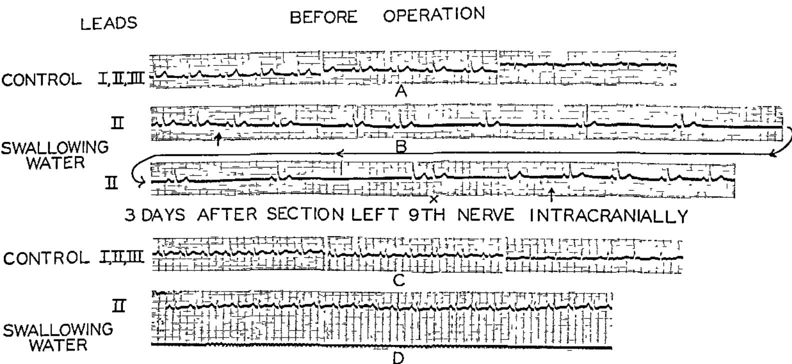


Fig 60

Electrocardiographic Changes in a Man 49 Years of Age who Had Glossopharyngeal Neuralgia

A and *B* were taken June 21, 1946 before section of 9th nerve intracranially the same day *A* shows three standard leads as a control taken on June 21 1946 *B* shows a long strip of Lead II taken immediately after *A* to demonstrate the effect of taking a swallow of water The first arrow indicates the time at which the patient swallowed, the second arrow when he finished Marked slowing of heart with sinus bradycardia (16 per minute) followed by asytole for 3 8 seconds, with ventricular escape in QRS complex before X This was followed by retrograde conduction with auricular premature contraction, X, then another ventricular escape, after which there was return to normal rhythm when swallowing was completed Swallowing was followed by pain, and asystole with dizziness and fall in blood pressure

C and *D* show electrocardiographic studies made June 24, three days after section of left 9th nerve *C* records the three standard leads as a control *D* shows Lead II, made immediately after *C* to illustrate the effect of swallowing The signal at the bottom of the record indicates when swallowing started and ended There was no change in heart rate The patient has experienced no recurrence of pain and dizziness (Ray, B S, and Stewart, H J Glossopharyngeal neuralgia A cause of cardiac arrest *Am Heart J* 35 458, 1948)

The diagnosis is made on auscultation of the heart and palpation of the pulse during a spontaneous attack of pain or during one induced by swallowing. Pressure over the carotid sinus on the affected side may induce pain, while pressure over the normal side will be painless Confirmation of the cardiac mechanism during the pain and syncope can be obtained in electrocardiograms taken during an attack (Fig. 60)

TREATMENT

Temporary Measures

Cocainization of the posterior portion of the tongue and pharynx may diminish the degree of pain or abolish it. Procainization of the carotid sinus on the side of the pain may be expected to prevent the cardiac arrest and syncope but to have no effect on pain Atropinization of the patient will probably prevent cardiac arrest with the associated fall in blood pressure and syncope, but is not to be expected to alter the pain

Surgical Measures

Intracranial division of the ninth nerve gives relief from the pain and abolishes the attacks of cardiac arrest and syncope The operative procedure is carried out in exactly the same manner as for the treatment of the hypersensitive carotid sinus (Ray) (p 470) Following waking from the anesthetic there is no return of the neuralgia. Swallowing does not cause pain, cardiac arrest, or change in heart rate (Fig. 60) Pressure over the carotid sinus on the involved side now causes no pain and no change in heart rate or blood pressure. There is anesthesia of the base of the tongue, the palate, and the pharynx in the region supplied by the sectioned glossopharyngeal nerve, but the patient is unaware of the sensory loss Convalescence from the operation is rapid and discharge from the hospital is permitted in seven to ten days.

Tonsillectomy is of no permanent benefit in controlling the pain.

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CHAPTER 27

Heart Disease in the Aged

CARDIOVASCULAR CHANGES IN THE AGED

The heart muscle does not regenerate, and if we consider the unceasing activity of this organ—which beats more than three billion times in a life span of seventy years—it is to be expected that this system should be one of the most susceptible to the effects of old age. Clinical experience has been that arteriosclerotic and myocardial changes are the most frequent signs of the old age of the cardiovascular system the one demonstrating the loss of elasticity in the older tissues, the other showing the effects of the continuous activity of the heart muscle which derives its nutrition from a blood flow which is becoming restricted The majority of patients with other types of heart disease do not survive into the later decades, nor do those with significant congenital heart disease. I have, however, seen one patient with coarctation of the aorta accompanied by marked hypertension live to his sixty-ninth year only to die of carcinoma of the larynx Dr George J. Heuer performed a pericardiectomy on one of my patients with chronic constrictive pericarditis with calcification who was 57 years of age. I have recently seen a patient with *mitral stenosis, mitral insufficiency, aortic stenosis and insufficiency, auricular* fibrillation, and heart failure at 72 years of age recover a fair functional capacity with restoration of compensation and maintenance on a sensible cardiac regimen There are other reports of survival of patients with mitral stenosis far beyond 50 years of age Most patients with rheumatic heart disease, however, do not attain such longevity. The same is true of syphilitic heart diseases, namely aneurysms and aortic insufficiency Nor is such longevity achieved by most patients who have suffered from arterial hypertension, with elevation of the systolic and diastolic blood pressures. On the other hand, patients with arteriosclerosis and systolic hypertension survive into the older age periods Persons who have escaped these manifestations in their middle years may show such aging phenomena in their later

years. The rise in systolic blood pressure with aging is an accompaniment of the inelasticity of the arterial system and may serve as a compensatory mechanism.

Physiologic Versus Pathologic Changes

For the most part adequate studies have not been made which would justify our stating which changes are those of normal aging and which changes represent disease in an older person We know that certain persons attain very old age with a normal blood pressure, without gross enlargement of the heart, and without symptoms referable to the cardiovascular system. Such objective records as the electrocardiogram may also be within the normal range. There are trends toward certain functional and anatomic changes in the cardiovascular system with advancing years: The systolic blood pressure rises slowly from the fourth to the sixth decade, after which there is a more rapid elevation. On the other hand, the diastolic pressure falls slightly if hypertension is not present, so that the pulse pressure increases. The heart size according to x-ray examination may increase slightly; there may be slight fullness of the left ventricle; the aorta may be elongated and the aortic knob may be prominent; calcification of the aortic knob, of the mitral and aortic valves, and rarely of the coronary arteries may be seen The peripheral vessels may show thickening, and rings of calcification may be palpated.

The *electrocardiogram* does not show a typical pattern for the aging heart, and may not differ from that of a young person There may be a tendency toward lowering of the amplitude of the QRS complexes as well as of the T waves in older subjects. Left axis deviation is common Right axis deviation is uncommon and in each instance requires adequate explanation With the increase in amplitude of the downward deflection of the QRS complexes in Lead III, the T waves may become negative Inversion of the T waves may occur in other leads. Partial auriculoventricular heart block and bundle branch block occur Complete heart block and the Q-T patterns of myocardial infarction indicate more serious myocardial damage. On the other hand a patient may show serious organic heart disease in the presence of a normal electrocardiogram or of one that does not fully reflect the gravity of the cardiac condition. The electrocardiogram must therefore be viewed as a part of the whole clinical picture.

There is increase in sensitivity of the *carotid sinus reflex* with advancing age.

The *cardiac output* expressed as liters per square meter of body surface per minute —the cardiac index—decreases slightly with advancing years. This is attributed to the decrease in basal metabolic rate with aging. The *vital capacity* decreases, reflecting the change in the structure and function of the thorax and pulmonary system The *venous pressure* is normal The *circulation time* shows a moderate prolongation. The sedimentation rate rises slightly. The ability of the *kidneys* to clear the blood of urea declines, and the urea nitrogen content in the blood increases The concentrating ability of the
be decrease in the amount of acid secretec
gastric, and pancreatic *secretions* (except amylase). [illegible]
artificial stimulation. There is a lack of correlation between age and levels of blood lipids and cholesterol, but this does not mean that there is no change in lipid metabolism with aging.

as chronic emphysema, chronic bronchitis, and asthma.

The examination of the elderly individual does not differ from that of a younger one. Care must be exercised not to engage in too exhausting or too prolonged examinations at any one time. How much the patient is able to do is a good guide to his functional capacity. There are certain over-all observations that give an indication of the aging of the individual with respect to the stated age: arcus senilis, graying of the hair and its sparseness, thickness of the skin, and loss of weight, of the vigor of the voice, and of the spring of the gait.

The treatment of cardiovascular ailments in the aged *does not differ significantly* from that accorded younger patients. It may be better not to keep older individuals in bed longer *than absolutely necessary, in order to prevent them from becoming* bedridden and to obviate the risks of pulmonary complications such as bronchopneumonia. The introduction of antimicrobial agents has provided greater margins of safety in the treatment of infections.

CARDIAC LESIONS OF THE AGED WHICH REQUIRE TREATMENT

Older patients are spared certain varieties of cardiac disease However, if they have *rheumatic heart disease*, they are still subject to all the hazards to which patients suffering from this type of heart disease are prone—congestive heart failure, auricular fibrillation, and *subacute bacterial* endocarditis being the most common. Patients with calcific aortic *stenosis* may suffer from congestive heart failure, angina *pectoris, and subacute bacterial endocarditis. Rarely mitral stenosis may be due to* arteriosclerotic changes. In older patients with valvular defects the consequences of congestive heart failure may be more severe than in younger individuals, owing to the effects of aging on the coronary arteries and on the myocardium, as well as to senile pulmonary changes

Subacute bacterial endocarditis superimposed on calcific or bicuspid aortic valves and on valvular damage in older rheumatic patients should be suspected when low-grade fever, malaise, and gradual deterioration in health are encountered.

Aged patients may have *angina pectoris* associated with coronary arteriosclerosis. *Angina of effort may be aggravated* by anemia. These persons are subject to myocardial infarction due to coronary thrombosis, but infarction may occur without thrombosis. They may *suffer rupture of the aorta or of an arteriosclerotic aneurysm.*

Older patients may have abnormal rhythms in association with valvular disease, with coronary artery disease, and with coronary thrombosis (Chapter 5). Conduction defects may be recorded in electrocardiograms. Most instances of acquired complete heart block are due to arteriosclerotic changes in the vessels supplying the septum of the heart. Ventricular premature contractions are common. Auricular fibrillation may occur. Paroxysmal tachycardia of ventricular origin is more common than any of the supraventricular types.

TREATMENT

Congestive Heart Failure

Heart failure in the aged may result from valvular disease which is rheumatic or arteriosclerotic in origin, generalized coronary artery disease, old or recent myocardial infarction, hypertension, pulmonary heart disease, or a combination of several of these factors It may be precipitated by the onset of paroxysmal tachycardia, acute respiratory infections, hyperthyroidism, or unusually strenuous activity. Prevention of heart failure in this group of patients may be promoted by guiding their activities to avoid undue physical exertion and by prompt treatment of respiratory infections and other systemic disease Anemia and nutritional deficiencies should be corrected in order to avoid these extra strains on the aging heart.

The treatment of heart failure is no different from that given to younger patients: restriction of salt and of fluid intake, and administration of digitalis, mercurial drugs, ammonium chloride, and oxygen. It may be expedient to be more liberal with the fluid intake if there is nitrogen retention, urinary infection, or fever. A daily allowance of 1500 to 1800 cc. is permitted, rather than 1200 cc. Digitalis is used in the same manner and in the same amounts as with other patients. I have not been impressed that toxicity from amounts in the therapeutic range of the drug occurs more frequently in patients in the older age group However, an amount of the drug which would be toxic for younger patients may produce toxicity more rapidly with old patients Nevertheless, with respect to the induction of premature contractions and of conduction defects, special warnings have been made about the use of digitalis in the aged.

Unless there is urgency, 0.5 to 1.0 cc of a mercurial diuretic should be given as the initial dose in order to avoid dehydration. For the same reason mercurial diuretics should be given at intervals of three days or longer, rather than daily Too vigorous diuresis should not be undertaken in older individuals with prostatic enlargement, because acute urinary retention may follow rapid distention of the bladder.

Morphine should be used with care in order to avoid depression of the respiratory center.

Patients who are acutely and severely ill should remain in bed in order to give as complete rest to the heart as possible. The bedpan should be used This regimen should be especially strict if heart failure is a consequence of acute myocardial infarction.

If congestive heart failure is moderate in degree a commode may be used at the bedside. If heart failure is not acute and has not reached alarming proportions, and there is the added complication of nitrogen retention, it may be advisable to allow the patient to sit up a short while once or twice daily. In the treatment of the more chronic form of heart failure with nitrogen retention, it may be expedient to allow patients to walk around the room slowly several times a day

The diet should be easily digested. Vitamin supplements may be used. A bowel movement should be obtained daily with mild cathartics when necessary.

From my own experience and from data which have been published, I see no

contraindications to keeping older patients at rest in bed when indicated; a few exceptions have just been mentioned. If the patient turns frequently, if he moves his legs often, if he does not lie with the legs crossed in a way to cause pressure, and if he is required to breathe deeply several times every hour to expand his lungs there need be no great apprehension about peripheral venous thrombosis or pulmonary embolism

As improvement occurs gradual ambulation is carried out.

Angina Pectoris

Angina of effort is treated as in other patients. Alcohol injection may be given consideration for a few patients. It does not appear appropriate to employ surgical measures for the relief of angina. The ordinary life expectancy in these later age periods is too short to subject patients to operations having known risks. If smoking means a great deal to the patient, its benefits in maintaining morale are weighed against the possible harm. Nitroglycerin may be used in anticipation of pain. The ingestion of an alcoholic beverage at frequent intervals may be used with benefit in doses which are compatible with the patient's tolerance Consideration may be given to the use of propylthiouracil or I^{131} to reduce the basal metabolic rate if it is elevated

Coronary Thrombosis

Myocardial infarction is treated as in other patients suffering from this accident (Chapter 13). For this group of patients, however, I recommend the minimal period at complete rest in bed that is compatible with the severity of the infarction. The rationale for this plan has been discussed under the treatment of congestive heart failure above.

This does not mean, however, that bed rest should be ended before healing is advanced. Patients have been seen in this age group who, having refused to accept the advice to remain in bed, have quite early developed signs and symptoms of chronic heart failure with intractable precordial pain Invalidism results, or convalescence is delayed for many months. From an estimate of the extent of the primary damage and of the state of the patient before the occurrence of the coronary thrombosis, a satisfactory recovery might otherwise have been expected. It may require all the physician's skill to persuade an older person who is having his first major illness to accept the necessary restriction

Subacute Bacterial Endocarditis

Subacute bacterial endocarditis is treated with penicillin or other antimicrobial agents as indicated (Chapter 22) Penicillin should be given regardless of whether the diagnosis is substantiated by blood cultures within a reasonable time.

Irregularities of Rhythm

The cardiac irregularities are treated in this age group as in other patients exhibiting these rhythms.

The management of rupture of the aorta and of dissecting aneurysm is the same as in other patients suffering these accidents.

SURGERY AND ANESTHESIA IN THE AGED

With the increase in life span and larger numbers of older patients, surgeons have had to alter their attitude about operating on older patients. It has been shown that patients in the later decades can sustain prolonged major surgical procedures if special care and skill are employed. The hazards increase, however, when the patient has a cardiac lesion The management of diabetes in the aged in relation to surgical events requires expert supervision.

Anesthesia

Few specific rules can be laid down about anesthesia in the aged. The anesthetic which is most appropriate for the operation and the status of the patient should be employed. Anesthetics which cause fall in blood pressure should be avoided, myocardial infarction and cerebral thrombosis may occur with the decline in blood *pressure With spinal anesthesia the judicious use of paredrine or neosynephrine is* appropriate to prevent a fall in blood pressure Ether and oxygen are satisfactory in patients with cardiac complications. Penicillin may be used to prevent pulmonary complications Cyclopropane finds wide use because high concentrations of oxygen can be employed, but it has the disadvantage that it frequently induces cardiac arrhythmias. premature contractions, ventricular paroxysmal tachycardia, and *ventricular fibrillation Pentothal sodium may be used intravenously if care is exer*cised not to induce too deep anesthesia

In a recent analysis Morrison concluded that the surgical risk is greater in patients with arteriosclerotic heart disease than in those with rheumatic heart disease Abnormal rhythms and poor renal function affected the risk adversely. No single anesthetic seemed to be superior for patients with heart disease. He advised that local anesthesia be used when circumstances were favorable, and that spinal anesthesia be avoided whenever possible

Infusions

More care is necessary in the use of intravenous fluids in older individuals than in younger ones with more resilient cardiovascular systems. Intravenous infusions are not required for all these patients during surgical operations. If the operation is such that hemorrhage may occur and a transfusion may be required quickly, it may be expedient to slow the intravenous infusion until the needle only just remains patent, the flow should be speeded up only if necessary. For other patients a hypodermoclysis may insure a slower restoration of fluid at a safer rate The amount of intravenous fluids after operations should be checked carefully so that no more is given than is necessary to maintain a fluid balance. Amounts as large as three, four, five, and six liters are usually not necessary. The chest *should be watched for* the appearance of râles and the neck veins for venous engorgement.

The use of one-sixth molar sodium lactate intravenously may lead to *alkalosis*, especially if there is continuous vomiting or if gastric suction is used. Marked renal impairment and decrease in amount of urine may occur with alkalosis. There may be personality changes, delirium, stupor, or convulsions (Grace and Barr). The carbon dioxide-combining power of the serum may be greatly elevated, the blood urea

nitrogen may be increased, and the serum chlorides decreased The dangers of precipitating alkalosis may be lessened by the simultaneous administration of sodium chloride. However, the addition of large amounts of sodium increases water retention and may lead to congestive heart failure. With increase in circulating fluids electrocardiograms may show the changes associated with acute cor pulmonale. Later there may be prolongation of the Q-T interval in electrocardiograms as evidence of hypocalcemia. At the same time muscle twitchings and positive Chvostek and Trousseau signs and carpopedal spasm may be elicited. On discontinuance of gastric suction and of the lactate, the symptoms and abnormal signs may clear, and the aberration in the blood chemistry may be corrected. It may be necessary, however, to use ammonium chloride intravenously or sodium chloride intravenously and ammonium chloride by mouth to achieve a more rapid restoration. Patients with emphysema are more easily made alkalotic by the use of lactate than are subjects whose lungs are normal.

Oxygen

The use of oxygen postoperatively will take some of the load off the heart in aged individuals. It may be beneficial if it is used routinely It should be required if there is evidence of cardiovascular damage before or during operation

Postoperative Mobilization

Early mobilization may be attempted postoperatively if the patient is not too sick The type of operation which has been performed is also a deciding factor Mobilization should be undertaken especially carefully if an aged patient has a history of congestive heart failure. On the other hand, patients with a known history of myocardial infarction in a satisfactory state of compensation require no particular schedule of mobilization Care is exercised to detect early evidences of decrease in functional capacity of the heart

In the surgical treatment and postoperative care of patients in this age group it seems important not to rely on standardized regimens Each patient should have each item in his treatment carefully adjusted to his capacities By such foresight, difficulties can be avoided later

PHYSICAL MEDICINE IN THE AGED

Activity compatible with the functional capacity of the patient should be encouraged Slow return to activity should be instituted as soon as possible after illnesses. Excessive walking, lifting, and efforts requiring sudden expenditures of energy should be avoided Mild passive massage may be useful in maintaining muscle tone when activity is limited Injury to veins should be avoided when massage is given Most of the treatments given at spas are too vigorous for aged individuals. Hot and cold baths require too great alterations in the cardiovascular system to be used with safety A bath every other day may be adequate for older individuals if they are not incontinent and do not have body odors. Daily bed baths, even when carried out by competent nurses, may be too vigorous for many aged patients

SUMMARY

The arteriosclerotic forms of heart disease are encountered most commonly in the aged. The same principles apply in the treatment of cardiac complications in this age group as in the treatment of these forms of heart disease in younger individuals; only a few modifications are required. The aims should be to keep the aged patient active, return him to activity after illnesses, to try to keep him usefully occupied in order to avoid rapid mental and physical deterioration and to allow him to maintain his self-respect. One cannot help being impressed with the almost unlimited recuperative powers of the human organism even late in life, a factor which aids in carrying out these aims. Until recently infections were the complications most feared in the aged, but with the introduction of antimicrobial agents these hazards have been lessened Investigators who are interested in geriatrics are faced with many problems requiring resolution in a segment of the population which is increasing in numbers.

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CHAPTER 28

Heart Disease and Pregnancy

The occurrence of pregnancy in patients with heart disease and the onset of cardiac disease during this state are the mutual concern of obstetrician and internist and require their close cooperation. Preventive medicine and routine medical examinations should play an important role in extending the life span of patients with heart disease in the childbearing period. Experience has shown that as many as 50 per cent of cardiac patients are unaware of the existence of their heart disease at the time they first consult a physician after the onset of pregnancy. All too often patients whose cardiac status contraindicates it become pregnant. Frequently this occurs because the physician has not discussed the advisability of pregnancy with the patient. Female patients in their late teens who have rheumatic heart disease or congenital heart disease should be guided in the matters of marriage and of pregnancy. They should be advised to submit to check-up examinations, consultations, and counseling interviews before marriage and then again before planning pregnancy. If patients are first seen after the beginning of pregnancy, the situation then has to be met as the month of pregnancy and status of the heart disease dictate.

DYNAMICS OF THE CIRCULATION IN PREGNANCY

Circulatory changes in normal women during pregnancy have been studied by Stander and his associates, and by Burwell. Such alterations are apparent around the fifth month of pregnancy and are at the maximum around eight and one-half months. The following changes take place: increase in blood volume, increase in minute volume output of blood by the heart, increase in oxygen consumption, and decrease in arteriovenous oxygen difference. Burwell draws the parallel between these changes and those prevailing in the presence of an arteriovenous fistula. To these basic changes are later added the increased demands of labor. Sampson, Rose,

and Quinn have estimated that the work of labor in both primiparous and multiparous women is the equivalent of mild to moderately heavy physical labor and cannot be predicted for any one patient.

The physiologic changes in the circulation during and after obstetric labor have been studied by Brown, Sampson, Wheeler, Gundelfinger, and Giansiracusa. Their results were consistent with, but did not prove conclusively the hypothesis that an arteriovenous shunt of considerable proportions exists in the pelvis at term and that its obliteration by delivery may contribute to the load on the cardiovascular system. The changes in heart rate, blood pressure, vital capacity, and circulation time were not uniform and did not follow a consistent pattern. The venous pressure increased—often to abnormal levels—in the 24 hours after delivery, which might have been due to the use of ergotrate. They were therefore of the opinion that ergot derivatives as well as posterior pituitary preparations should be used with great caution in all patients with serious heart disease, especially in the presence of congenital intracardiac shunt. From their observations of blood volume and hematocrit levels it appeared (1) that fluid leaves the vascular system at the time of delivery, (2) that around the second day of puerperium a larger volume of fluid returns to the blood stream, and (3) that there is then a return to the normal nonpregnant blood volume following postpartum diuresis They were of the opinion that repeated uterine contractions during labor temporarily increase the blood volume and that intermittent occlusion of the placental circulation prepares the cardiovascular system for permanent occlusion of the shunt For this reason they think that vaginal delivery is tolerated by patients with serious heart disease as well as or better than cesarean section.

How then does the cardiac patient manage in the face of the demands which pregnancy requires in the normal women? This question is best answered by consideration of rheumatic valvular disease, which has been most studied from this point of view Stewart and associates found that the resting cardiac output per minute and the stroke volume are decreased in rheumatic valvular disease before the occurrence of heart failure. The reduction is least in patients exhibiting mitral stenosis and insufficiency, and aortic insufficiency, somewhat more in those suffering from mitral stenosis and insufficiency alone, and greater still in those having mitral stenosis and insufficiency, and aortic stenosis and insufficiency. During heart failure the minute and stroke volumes decrease further.

Hickham and Cargill have supplied data with respect to exercise, a matter of importance in this connection They showed that patients with valvular heart disease and congestive failure were unable to increase their cardiac outputs to any extent when they exercised, in contrast to the increase in minute volume which occurs in normal subjects

From these studies it is apparent that patients with rheumatic valvular disease before the onset of failure might be able to meet the demands of pregnancy with a moderate increase in cardiac output per minute, but those who are in failure and to a less extent those who have experienced failure are unable to increase the cardiac output. It is not unexpected therefore that some patients with rheumatic valvular disease will experience diminution of cardiac reserve during pregnancy, or

develop heart failure, or suffer an aggravation of signs and symptoms of cardiac insufficiency.

The New York Heart Association Classification of Heart Disease, based on etiologic, anatomic, physiologic, functional, and therapeutic criteria, provides some degree of uniformity in thinking about patients with heart disease. The functional capacity is of especial importance in relation to pregnancy. The separation of patients into the functional groups is difficult because there are no objective, clinical tests available at present Consequently the groups are established on the basis of signs and symptoms Nevertheless within certain broad limits patients in the same functional rubric behave in a consistent fashion in response to pregnancy, although too much emphasis should not be placed on this and treatment should always be individualized.

RHEUMATIC HEART DISEASE

Rheumatic heart disease is important in relation to pregnancy since this group accounts for more than 90 per cent of pregnant cardiac patients. When advice is sought about the advisability of pregnancy, examination should be made to identify the valve lesions and to estimate the functional capacity of the patient Advice of an obstetrician should also be enlisted The age of the patient is important Whereas [illegible] pregnancy, [illegible] erms of the [illegible] f pregnancy and the labor are usually easier, factors which are taken into consideration in arriving at an opinion. There is reason to believe that a young patient who has not suffered from a rheumatic infection for some time and has experienced no signs or symptoms of cardiac insufficiency can sustain pregnancy without accident.

A patient having aortic stenosis and insufficiency and mitral stenosis and insufficiency should be advised against becoming pregnant Studies by Stewart and associates made of patients with this combination of valve defects have shown a marked decrease in functional capacity. Patients with tricuspid stenosis and insufficiency should not become pregnant

Patients in whom auricular fibrillation is the established rhythm should not become pregnant.

Careful medical supervision is essential during pregnancy Colds should be prevented if possible; when they occur the patient should remain in bed Heart failure is often precipitated by the strain of an acute respiratory infection It is treated in the manner customary for that condition Streptococcal infections should be treated with penicillin and the patient observed closely to detect recurrence of rheumatic infection. The activities of the patient should be restricted if she demonstrates any decrease in functional capacity

If the patient has suffered from congestive heart failure, if the heart is greatly enlarged, or if digitalis has been required before pregnancy, therapeutic abortion is usually the safest recommendation provided the patient is seen early enough. When pregnancy is allowed to continue the patient should be seen more frequently as the pregnancy advances. At times we have felt concern when unusually large amounts

of digitalis were required to control auricular paroxysmal tachycardia. There is no indication that digitalis is transferred in toxic amounts to the fetal circulation when it is used in the usual therapeutic amounts. Slowing of fetal heart rate has not been encountered as a sign of toxicity. The fetal heart rate may be recorded in the maternal electrocardiogram by placing electrodes over the abdomen and taking the electrocardiogram with the galvanometer string loosened. It may be wise for the patient to be at rest in bed during the last months of pregnancy; hospitalization with close supervision may be required.

The ultimate effect of pregnancy on the patient suffering from rheumatic heart disease has not been accurately delineated in the light of adequate series of reported cases. The hazard can be greatly lessened by the cooperation of internist and obstetrician in charge of the patient. The average life expectancy may not be shortened by pregnancy. But these statistics do not allow a prediction about the individual patient It is a common experience to see patients whose functional capacities have been greatly and permanently reduced by pregnancy. The life span of female patients with rheumatic heart disease has a wide range and it is difficult to compare a group which has not borne children with a group who have experienced pregnancies in such a way that the statistics are valid.

If the decision has been made to allow pregnancy to continue, the question arises whether to allow spontaneous delivery or to resort to cesarean section. This is discussed on page 495.

Penicillin in adequate amounts should be used during labor and for a few days afterward as a precaution against subacute bacterial endocarditis.

CONGENITAL HEART DISEASE

Approximately 2 per cent of the cardiac patients who become pregnant suffer from congenital heart disease.

An accurate appraisal of the anatomic lesion and the functional capacity should be attempted. Visualization of the heart cavities by angiocardiography and right heart catheterization may be indicated One must be especially alert for the appearance of subacute bacterial endocarditis during and after pregnancy The second stage of labor should be shortened by the use of forceps Local anesthesia at delivery may be used to minimize the loss of blood during the third stage.

Penicillin should be used in adequate amounts during labor and for a few days afterward as a precautionary measure, to guard against subacute bacterial endocarditis

Patent Ductus Arteriosus

Many patients with patent ductus arteriosus appear to go through pregnancy without embarrassment. On the other hand because of the increased work of the heart in this congenital defect, plus the added work consequent to pregnancy and, finally, because of the increased demand during labor, pregnancy is generally contraindicated unless, perhaps, the ductus is small in caliber. If the patient is seen before pregnancy occurs the procedure of choice would be ligation of the ductus,

if this is possible (Chapter 6). Success in this surgical procedure would, of course, remove any objections to pregnancy after the period of healing.

Treatment

If the patient is first seen after she is pregnant, the same supervision is accorded as that given to patients with rheumatic heart disease.

COARCTATION OF AORTA

I think it is best for women with coarctation of aorta not to become pregnant, especially if the blood pressure is greatly elevated. A few patients with coarctation of the aorta do not survive pregnancy and about half of those who survive experience deleterious effects from the pregnancy. Before pregnancy surgical resection of the defect and end-to-end anastomosis of the two ends of the aorta might be recommended provided there are no contraindications (Chapter 6), although as yet there are no reports of pregnancy after this procedure. When there is a great desire to have a child, the risk might be taken if the blood pressure is only moderately elevated, but the risk should be explained to the patient and her husband.

Treatment

If patients are seen for the first time early in pregnancy the symptoms, blood pressure, previous pregnancies, and the ease of the labor in them should form the basis for deciding whether to interrupt the pregnancy or allow it to go to term It might be permissible to carry on until a viable baby can be obtained by cesarean section Patients seen late in pregnancy are carried along under close supervision, at complete rest in bed, until delivery The appearance of aortic insufficiency after labor in certain of these women is evidence that irreversible distention of the aorta above the constriction has occurred. All of the accidents to which patients with coarctation of the aorta are prone have been reported in pregnancy.

Delivery should be accomplished by cesarean section in order to avoid the prolonged strain of labor If spontaneous labor is decided upon, delivery should be made when the cervix is fully dilated and the head is on the perineum, in order to avoid the work of bearing down during the second stage of labor

PULMONARY STENOSIS

Patients with uncomplicated pulmonary stenosis have sustained normal pregnancies, normal deliveries, and normal puerperia. If the exact diagnosis is not clear, angiocardiograms and possibly venous catheterization of the heart may form the basis for recommendations. When patients are seen after the onset of pregnancy they are kept under careful supervision Any change in functional capacity would be occasion to prescribe bed rest, digitalis, and other measures. Decision would then be made whether to continue pregnancy.

INTERVENTRICULAR SEPTAL DEFECT AS AN ISOLATED LESION

Patients with small interventricular septal defects have minimal disturbances of cardiac physiology and sustain pregnancy in a normal manner. Those with large

left-to-right shunts may suffer decrease in functional capacity and may require special supervision. The strain of labor may upset the balance which has been established to take care of the shunt.

Congenital Heart Disease with Cyanosis

Patients who have cyanotic forms of heart disease due to pulmonary valvular stenosis with or without intracardiac shunt should be advised against pregnancy. Patients exhibiting intracardiac shunts such as occur in the tetralogy of Fallot provide an insecure background on which to graft the added demands of pregnancy In this instance the right-to-left shunt which prevails before pregnancy might be greatly altered by the changes in the dynamics of the circulation during pregnancy Interruption of the pregnancy is usually indicated when the patient is seen early. Should patients be examined for the first time after pregnancy is well advanced, they are kept under supervision and treated in a manner similar to that described for patients with rheumatic heart disease. Certain of these patients with evidence of minimal valvular deformities compatible with the diagnosis of pulmonic stenosis have gone through normal pregnancies, normal deliveries, and normal puerperia

Dextrocardia

Patients with dextrocardia go through pregnancies in a normal fashion. If, however, this defect is combined with other associated congenital cardiac abnormalities pregnancy might be inadvisable.

HYPERTENSION

Most women with essential hypertension, or hypertension which is the consequence of nephritis, should be advised not to become pregnant, especially if the blood pressure is significantly elevated Not only is pregnancy prone to complications for the mother, it may not be possible to secure a living child if there is progression of the hypertension during the course of pregnancy. During pregnancy the progress of the disease may be accelerated, or latent symptoms may become manifest.

Cardiac changes have been described in toxemia of pregnancy. Heart failure may occur The electrocardiogram may show transient alterations which are like those seen in myocardial infarction. Focal myocardial necrosis has been reported

Treatment

If the patient is first seen when already pregnant and the blood pressure is not at alarming levels, the pregnancy is allowed to continue provided the renal function is satisfactory, the blood urea nitrogen is not elevated, there is no albuminuria, no eyeground changes, exudate, papilledema, or retinal arteriosclerosis. The status of the patient is followed carefully Interruption of the pregnancy may be necessary if there is any change in the patient's condition The complications may be predominately renal or cardiac. Therapeutic abortion is indicated for patients with marked elevation of blood pressure in the presence of reduced renal function and cardiac symptoms. If continuation of pregnancy is in order, adequate rest should

be imposed, in the hospital if necessary. Complications are treated as with other cardiac patients during pregnancy.

Pregnancy is contraindicated and should be terminated in the presence of chronic nephritis, unless the disease is mild, when it may be allowed to continue under close observation If the patient is first seen late in pregnancy, she should be put to bed and carefully observed. Cesarean section with sterilization may be indicated for a few patients Spontaneous delivery may be possible for most patients, with tubal ligation two to three days later.

Pregnancy Following Splanchnic Resection

Women who have had lumbodorsal sympathectomy for hypertension should be advised not to become pregnant even though the blood pressure has fallen permanently to normal levels Too few follow-up studies have been made for us to be able to give a prognosis for any particular individual. When the blood pressure of the hypertensive patient has been reduced to normal levels, all measures should be directed at maintaining the status.

The operation has also been carried out in only a few patients early in pregnancy Experience relating to patients who have become pregnant after sympathectomy has also been limited Some of these patients sustain pregnancy without any overt complications and without apparent alteration of the renal and cardiac functional capacities. The blood pressure may remain unchanged or temporary rises may occur during pregnancy. Therapeutic abortion should be carried out if it appears indicated by changes in the patient's condition In the long run it may have been better if these patients had not gone through pregnancy

MYOCARDIAL INFARCTION

Fortunately the complication of coronary thrombosis in pregnant women and the problem of pregnancy after this accident do not occur frequently. This cardiac disorder is rarely encountered in women in the childbearing age.

Women who have had a myocardial infarct should be advised against pregnancy Should the infarct occur during pregnancy, bed rest and the other customary measures are employed There is, however, one phase of treatment which requires special consideration: the use of anticoagulants, with which there has been little experience under these circumstances. If there are indications that the area of infarction is small, it might be well not to use anticoagulants In this case the patient should be turned frequently, should take frequent deep breaths to avoid pulmonary stasis, and move her legs to avoid venous stasis of the lower extremities.

Anticoagulants

If there are evidences of more serious cardiac damage with a larger area of involvement and more marked systemic reaction, anticoagulants should be used as described in Chapter 4. Care should be exercised to keep the prothrombin level at the lower limits of the optimal range. If the program for the use of an anticoagulant promises to overlap the time of delivery, it might be well to discontinue the drug two days before the expected date and resume it afterward Tromexan might be

be imposed, in the hospital if necessary. Complications are treated as with othe cardiac patients during pregnancy.

Pregnancy is contraindicated and should be terminated in the presence o chronic nephritis, unless the disease is mild, when it may be allowed to continu under close observation. If the patient is first seen late in pregnancy, she should b put to bed and carefully observed. Cesarean section with sterilization may b indicated for a few patients Spontaneous delivery may be possible for most patients with tubal ligation two to three days later.

Pregnancy Following Splanchnic Resection

Women who have had lumbodorsal sympathectomy for hypertension should be advised not to become pregnant even though the blood pressure has fallen per manently to normal levels. Too few follow-up studies have been made for us to be able to give a prognosis for any particular individual. When the blood pressure of the hypertensive patient has been reduced to normal levels, all measures should be directed at maintaining the status

The operation has also been carried out in only a few patients early in pregnancy. Experience relating to patients who have become pregnant after sympathectomy has also been limited. Some of these patients sustain pregnancy without any overt complicati
capacities.
during preg
by changes in the patient's condition In the long run it may have been better if these patients had not gone through pregnancy.

MYOCARDIAL INFARCTION

Fortunately the complication of coronary thrombosis in pregnant women and the problem of pregnancy after this accident do not occur frequently This cardiac disorder is rarely encountered in women in the childbearing age.

Women who have had a myocardial infarct should be advised against pregnancy. Should the infarct occur during pregnancy, bed rest and the other customary measures are employed There is, however, one phase of treatment which requires special consideration the use of anticoagulants, with which there has been little experience under these circumstances. If there are indications that the area of infarction is small, it might be well not to use anticoagulants In this case the patient should be turned frequently, should take frequent deep breaths to avoid pulmonary stasis, and move her legs to avoid venous stasis of the lower extremities.

Anticoagulants

If there are evidences of more serious cardiac damage with a larger area of involvement and more marked systemic reaction, anticoagulants should be used as described in Chapter 4. Care should be exercised to keep the prothrombin level at the lower limits of the optimal range. If the program for the use of an anticoagulant promises to overlap the time of delivery, it might be well to discontinue the drug two days before the expected date and resume it afterward. *Tromexan might be*

ities come about gradually, adjustments are made which allow the circulation to be maintained adequately; accordingly many of these patients manage satisfactorily in early life. However, cardiac symptoms and heart failure become common later. Heart failure in these subjects is spoken of as "pulmonocardiac failure." While the vital capacity is diminished in patients with marked deformity, the amount of activity they can tolerate without symptoms is astonishing. On the other hand, once symptoms have appeared they are persistent, and chronic heart failure may result with a narrow margin of functional capacity. To this heart failure may be added burdens of frequent respiratory infections. Acute bronchitis is especially common.

Treatment

Some patients with chest deformities, even when the maximal vital capacity is reduced to 1100 cc., will sustain normal spontaneous deliveries and normal puerperia without any untoward effects and without developing heart failure. When patients are seen during pregnancy, the state of the circulation together with the symptoms should be the deciding factors in planning the course. If pregnancy is allowed to continue a regimen is set up which aims to relieve the heart of as much work as possible. The method of delivery is decided at the appropriate time. For other patients interruption of the pregnancy by therapeutic abortion or cesarean section is advised. Sterilization should be carried out.

When these patients show marked deformity they should be advised not to become pregnant. It is difficult to establish criteria because so few of these patients are seen in a single clinic. The whole situation has to be considered: the chest deformity and its consequences on the cardiovascular system, as well as the associated deformity of the pelvis and the space available in the abdominal cavity for the expanding uterus. The symptoms of cardiac insufficiency, the predisposition to respiratory infections, and the history of failure are used in arriving at decisions.

EMPHYSEMA AND ASTHMA

Emphysema and asthma are mentioned briefly because the difficulty which arises in pregnancy in these patients pertains to the heart, namely heart failure of the high output variety. In the presence of marked emphysema in which the patient has symptoms before pregnancy or symptoms begin to appear during pregnancy, the pregnancy should be interrupted. The onset of heart failure is treated promptly and vigorously with the usual measures. Asthmatic attacks are treated in the usual manner. Asthmatic patients may be free of attacks during pregnancy.

CARDIAC IRREGULARITIES

Cardiac irregularities arising during pregnancy are treated in the same manner as when they occur under other circumstances. It is rare that abnormal rhythms merit anything but temporary alarm during pregnancy.

The management of pregnancy in patients with auricular fibrillation in rheumatic heart disease has already been briefly mentioned. Patients with chronic auricular

CARDIOVASCULAR SYPHILIS

Pregnancy does not often present a problem in cardiovascular syphilis. Syphilitic infection commonly occurs in the early twenties, and the cardiovascular manifestations appear approximately 20 years later when patients are more than 40 years of age. Moreover the incidence of cardiovascular syphilis in women is low.

SUBACUTE BACTERIAL ENDOCARDITIS

When subacute bacterial endocarditis is encountered during pregnancy it is treated vigorously in the usual manner. Special concern is directed to the state of compensation At the time of delivery extra weight is given to the mechanical damage which might have occurred during treatment of the endocarditis and to the possibility of heart failure on this basis when the extra load of delivery is imposed.

Davis and Wortmann report the case of a patient being treated for subacute *bacterial endocarditis with penicillin at the time of delivery by cesarean section of a* living baby. The following penicillin levels were recorded at the time of delivery. maternal blood, 2 048 units per cc, cord blood, 0 512 units per cc.; and amniotic fluid, 4.096 units per cc The organism *Streptococcus salivarius* was sensitive to 0 02 units of penicillin per cubic centimeter.

As increasing numbers of patients have been cured of subacute bacterial endocarditis the question has arisen of the advisability of these patients becoming pregnant later In the majority of cases I would strongly advise against pregnancy, because of the combination of the original cardiac defect with whatever additional deformity the process of healing and scarring may have induced The latter may be an unknown quantity until stress is placed on the heart. This recommendation would apply especially to patients with rheumatic valvular disease and to those with the more complex congenital defects. Patients with simpler congenital abnormalities such as small interventricular septal defects would be accorded a more lenient attitude. The decision in each case must be based on the available data and the estimation of the functional capacity of the patient.

To allow for relapse or for healing and scarring to have been completed, pregnancy should be deferred until six months to one year after recovery. The cardiovascular status should then be evaluated with respect to the advisability of pregnancy.

If pregnancy occurs after recovery from subacute bacterial endocarditis the management is based upon the same principles that guide the treatment of other patients with organic heart disease who become pregnant

CHEST DEFORMITIES

When the chest is greatly deformed by curvatures of the spine the pulmonary space is markedly reduced and encroached upon, and the heart and great vessels may be distorted and displaced from their normal location. Because these deform-

heart or other diseases which made this course inadvisable. Patients with bundle branch block of the S wave type could in most instances continue pregnancy especially if it were known that the bundle branch block had been of some years' duration and had not changed its configuration.

Wolff-Parkinson-White Syndrome

The Wolff-Parkinson-White syndrome is by itself no contraindication to pregnancy. Attacks of paroxysmal tachycardia would have to be properly appraised with respect to their effect on pregnancy. It is recalled that in patients with this syndrome paroxysmal tachycardia may be resistant to treatment.

SPONTANEOUS DELIVERY *VERSUS* CESAREAN

When a patient is first seen late in pregnancy, close supervision is maintained until term and spontaneous delivery or until a living baby can be obtained by cesarean section When a decision has been made in favor of continuing the pregnancy, the question then arises whether to wait for spontaneous labor or to resort to cesarean section In choosing the course to take, one must keep in mind the changes in the dynamics of the circulation during pregnancy and labor. If the patient has reached term without serious cardiac difficulty, spontaneous labor may be permitted without undue apprehension provided careful observation is maintained to detect the early evidences of heart failure.

Prolonged spontaneous labor should not be permitted. Delivery should be made when the cervix is fully dilated and the head is on the perineum in order to avoid as far as possible the work of the bearing down efforts of the second stage of labor Local anesthesia may be used to minimize the loss of blood during the third stage
failure the patient is immediately
carry the danger of the unpredict-
In deciding upon cesarean section
one should recall that in general cardiac patients tolerate surgery well, and that ether with oxygen is the general anesthetic which is best tolerated The trend at present is away from cesarean section and toward spontaneous delivery with a shortened labor and with regional anesthesia.

Operation or delivery should be carried out with the patient propped up During and after operation or spontaneous delivery as well as during convalescence careful medical supervision is necessary. Care should be exercised in the postoperative use of intravenous fluids in order not to induce acute heart failure Digitalization and other measures to combat heart failure should be promptly instituted as the need arises

TREATMENT OF CARDIAC EMERGENCIES DURING DELIVERY

Heart Failure

If the patient begins to show signs of heart failure or of acute pulmonary edema during delivery, ouabain or lanatoside C together with aminophyllin should be

fibrillation should be advised against pregnancy because of the possibility of *auricular mural thrombi*, a complication which is especially feared in patients with rheumatic heart disease. If the *patient is seen* early enough in pregnancy therapeutic abortion is usually the wisest procedure If pregnancy is continued or the patient is *first seen late* in pregnancy, the ventricular rate is kept slow with adequate ration doses of digitalis. Careful observation is maintained for the detection of *signs of* cardiac insufficiency. Hospitalization may allow continuance to term or until a viable baby can be obtained by cesarean section.

Most *paroxysmal rhythms* can be terminated quickly by the usual therapeutic methods and in many instances subsequent attacks may be prevented Only rarely is *paroxysmal* rhythm a cause for consideration of therapeutic abortion. If the *patient has* repeated attacks which are stubborn and do not respond readily to medical treatment, cervical sympathectomy might be considered. Certain patients with normal hearts have attacks of paroxysmal tachycardia only during pregnancy and the paroxysms may even become more frequent as pregnancy advances. I have not, however, encountered a patient in whom the attacks could not be controlled and in whom pregnancy could not be permitted to go to term. This is not to say that situations may not arise in patients with damaged hearts with prolonged and persistent paroxysmal rhythms which demand therapeutic abortion.

Complete Heart Block

Campbell has recently pointed out that congenital complete heart block is not so uncommon as it was formerly thought to be. It may, however, be overlooked because the ventricular rate may be more rapid than in the acquired type of complete heart block. The rate may be between 50 and 56 per minute. Some patients in Campbell's group had active service in the armed services in World War II without difficulty. He was therefore of the opinion that the prognosis in congenital complete heart block may be good and that the condition is compatible with survival to old age, provided there were no complications carrying special risks of their own. If there were other associated congenital cardiac anomalies, such as a septal defect, the prognosis would not be so good

Barton and LaDue have recently summarized the data relating to pregnancy in patients with complete heart block, and recommend that pregnancy be allowed to continue provided there are no associated congenital cardiac defects.

Bundle Branch Block

Bundle branch block is infrequent during pregnancy because this conduction defect is commonly seen in patients who are past the childbearing age Exceptions would be the incidence of bundle branch block in patients with long-standing or rapidly progressive hypertension with myocardial and arteriosclerotic damage Acquired bundle branch block, especially when a result of hypertensive cardiovascular disease, would be of grave import and would be a deciding factor in the discussion of therapeutic abortion However, it is recalled that the functional capacity of the heart may appear to be unimpaired in many patients with bundle branch block

Patients with congenital bundle branch block would be permitted to go through pregnancies as normal subjects unless there were other congenital defects of the

SUMMARY

In recent years the cardiac patient has been more satisfactorily treated during pregnancy, and maternal mortality in cardiac patients has been showing a satisfactory decline. This has resulted partly from the greater interest taken by obstetricians in the cardiac aspects of pregnancy, and partly from the efforts of clinics where cooperation among obstetricians, internists, and cardiologists prevails. The assignment to prenatal clinics of internists or cardiologists who guide the care of these patients while ambulatory, after admission to the hospital, through delivery, and then back to postnatal clinics also has been a rewarding effort

With the provision of proper medical and obstetric supervision, adequate rest, proper and prompt use of digitalis and other measures used in treating cardiac insufficiency, penicillin for infections, and prolonged hospitalization when indicated, patients with many cardiac diseases can now be brought safely through pregnancy. When cardiac and other emergencies occur they can be readily and quickly met Emphasis has also been placed upon advice to women suffering from cardiac disorders about the advisability of pregnancy The net result has been a gratifying reduction of maternal mortality in this group of patients

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given at once intravenously. An oxygen mask may be used. Delivery should be hastened by forceps if the head is well down and the cervix is fully dilated. Regional anesthesia should be employed.

Paroxysmal Tachycardia

Patients may have paroxysmal tachycardia during pregnancy and be free of attacks at other times In others paroxysmal tachycardia may come on during delivery. Patients who are prone to attacks of paroxysmal tachycardia of supraventricular origin and suffer repeated attacks during pregnancy might well be digitalized before delivery For other patients maintenance amounts of quinidine or pronestyl might be tried If paroxysmal tachycardia appears during delivery mechanical measures for ending it should be tried first. If the condition of the circulation seems satisfactory, if there are no signs of failure, and if delivery is imminent, it may be best not to try any medications such as quinidine intravenously or intramuscularly Experience with earlier paroxysms may be helpful in assessing the situation.

CARE OF THE CARDIAC MOTHER AFTER CHILDBIRTH

Ambulation

The continued observation and treatment of the cardiac mother after childbirth is an important part of the care of the patient If signs of cardiac insufficiency have not occurred during pregnancy or during delivery and if the patient has not been too distressed, early ambulation may be instituted. It should, however, be more slowly and progressively ordered If the patient has had heart failure or decrease in cardiac reserve, she should be treated as any other patient with heart failure, rest in bed being provided until the best possible state of compensation has been attained

When the mother has become ambulatory, her activities should be planned so that she may achieve a gradual building up to the level that she can attain without symptoms Expert advice may be needed in planning the care of the baby with the patient, as to how much she can do and what she must leave to others. Planning the housework and the regimen with respect to the use of stairs and other exertions requires consideration These matters cannot be dismissed with only the advice "not to do too much" The mother's medication and cardiac regimen should be carefully outined The mother should be seen at regular intervals afterward to be certain that she is remaining within the confines of her functional capacity, to be given advice about activities, and to detect any untoward results of pregnancy.

Nursing

In many instances there are no contraindications to the mother's nursing of the baby. It is easier on the mother and best for the baby if she does not attempt nursing should heart disease be advanced, should the mother's activities be restricted, should her regimen include a salt-poor diet and restriction of fluid intake so that she cannot drink an adequate amount of milk, and should medications be required. There is no indication that digitalis is excreted in the mother's milk.

CHAPTER 29

Cardiac Management of Surgical Patients

Patients in all age groups should be carefully supervised when they are subjected to surgical procedures so that cardiac complications may be prevented, or detected early, and to be certain that they are not precipitated by too vigorous therapy. In patients in the younger decades with normal hearts, the elasticity and adaptability of the cardiovascular mechanism are so great that the organ can compensate for great strains. In the middle and later decades the resiliency of the cardiovascular system is compromised and accommodation to stress is gradually lessened.

Each patient should be treated as an individual problem with respect to preoperative care, anesthesia, fluids during anesthesia, and postoperative care. In this regard a routine and a regimen do not replace judgment and do not obviate the provision of a basic plan adapted to the individual patient. Many of the pertinent facts relating to this subject are discussed in the chapter following this one.

TREATMENT OF COMPLICATIONS

Acute Heart Failure

One of the most common complications encountered is that of acute heart failure due to the overloading of the circulation by transfusions or by fluids. When saline infusions are used the retention of water more readily occurs. It is difficult to make any over-all statement about the amount of the fluid intake which should be given over a 24-hour period. An adequate output of nonconcentrated urine should be the goal. The amount of fluid must be adapted to the needs of the patient, the type and duration of operation, the amount of blood loss, and the medication being prescribed. The occurrence of shock is another factor to be considered. After operation the volume of fluid to be administered is determined by the volume of urine excreted, the amount of perspiration—the loss by insensible perspiration also being

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Thrombophlebitis

This complication may be prevented if the patient moves his legs and avoids lying in a position which obstructs the venous circulation Early ambulation also may prevent thrombophlebitis. I do not subscribe to the routine prophylactic ligation of the veins before operations—a practice employed in some clinics. It appears more expedient to use anticoagulant therapy, provided there are no contraindications.

Pulmonary Infarction

The pain, respiratory distress, and shock of pulmonary infarction may simulate coronary thrombosis. The former may be forestalled if after operation the patient is turned frequently and is induced to take frequent deep breaths. Early ambulation may prevent thrombophlebitis as a source of pulmonary emboli I have nevertheless seen patients suffer pulmonary infarction upon first sitting up when a plan of early ambulation was attempted. If pulmonary infarction occurs the patient should be kept in bed Oxygen may be required. Anticoagulant therapy should be instituted if there are no contraindications The electrocardiogram may help to distinguish this accident from myocardial infarction, provided it takes on the typical pattern of acute cor pulmonale

Pulmonary Atelectasis

Pulmonary atelectasis may be prevented by having the patient rebreathe 100 per cent oxygen, by turning the patient, and by aspiration of pulmonary secretions by suction If the patient is not too sick, pounding the chest may aid in coughing up a plug of mucus The cough reflex should not be lessened by the use of morphine and codeine Bronchoscopy for removal of a plug of mucus may be indicated to hasten recovery X-rays may be of indispensable aid in deciding upon the status of the lung

The management of this complication as well as of fluid in the pleural cavity or pneumothorax is more fully described in Chapter 30 Penicillin should be used to prevent infection The chest and abdomen should not be tightly bound

Cerebral Accidents

Thrombosis of a cerebral vessel may occur during fall in blood pressure resulting from anesthesia or from shock The current therapeutic trend is to start early ambulation and prompt attempts at re-education when the patient recovers consciousness and if paralysis is not extensive

Stasis Pneumonia

Prevention of this complication should be attempted by avoiding deep sedation after operation and by frequent turning of the patient. When it occurs the patient is given penicillin and kept in bed until he has recovered

Cardiac Irregularities

When cardiac irregularities arise they are treated as in other patients showing these rhythms The same modifications may be required as those discussed in

taken into account—the use of sulfonamides, and of one-sixth molar sodium lactate, and the loss of fluid by suction as with the Miller-Abbott tube. When fluids are being given parenterally venous distention and râles in the chest indicate early failure With rapid increase in blood volume, acute cor pulmonale may occur.

The electrocardiogram may show the sudden appearance of deep S waves which may be split in Lead I, a stairstep configuration of T_1 and T_2 and perhaps T_4, and increase in amplitude of the P waves. The pattern is not unlike that seen in pulmonary infarction The administration of fluids should be temporarily halted with the appearance of signs of heart failure or of acute pulmonary edema. When this situation arises it is treated as in other patients exhibiting acute heart failure aminophyllin intravenously, oxygen, digitalis intravenously, and one of the mercurial diuretics

The fluid intake is readjusted to levels commensurate with the improvement in the state of compensation. In many clinics attempts are made by estimation of the blood volume, pH and carbon dioxide content of the blood, and serum electrolytes, to supply fluids and electrolytes in proper amounts so that a normal balance is maintained In most instances a fluid intake of 2000 to 3000 cc. in 24 hours is adequate. It is indeed a strong heart that can accommodate itself to such colossal amounts of fluid as 6000 cc. a day—together with sulfadiazine to combat pneumonia and sodium bicarbonate to prevent crystalluria—even in the absence of the stress of a surgical procedure Heart failure is not uncommon when such regimens are instituted

Disturbance of Electrolyte Balance

This problem will be discussed in Chapter 31 The hazards are essentially the same as for patients with normal cardiovascular systems. alkalosis, hypocalcemia, sodium retention or sodium loss, and hyperpotassemia and hypopotassemia

Myocardial Infarction

Patients with apparently normal hearts may sustain myocardial infarction either with or without coronary thrombosis, because of fall in blood pressure during anesthesia or with shock (resulting from operation or blood loss)

It may be necessary to terminate or shorten the projected operation if one of these accidents should occur The shock should be combated with a minimum of intravenous fluids or plasma When myocardial infarction occurs the patient is kept at rest in bed after operation and is treated as any other patient suffering from coronary thrombosis, early ambulation being avoided. Immediately after operation the route of fluid administration has to be adapted to the state of the patient and the operation which has been performed

The electrocardiographic pattern of myocardial infarction which I have seen in a lad 11 years of age following gangrene and rupture of the appendix requiring drainage exhibited a series of changes over a period of months. In the absence of detectable cardiac anomaly, of hypertension, and of evidence of coronary artery arteriosclerosis in this young patient, I believed that he had sustained a coronary embolism. He has led a normal life since the episode.

CHAPTER 30

Surgery in Patients with Heart Diseases

Although patients with organic heart disease do surprisingly well when subjected to surgical procedures, management should not be routine. Each step in the procedure should be individualized, with special consideration given to anesthesia and to management before, during, and after operation.

PREPARATION OF PATIENT FOR OPERATION

Heart Failure as a Factor

If the patient has never suffered from heart failure, special preparations are unnecessary If on the other hand the patient has congestive heart failure, even though he is already on a cardiac regimen, a few days should be allotted to active therapy and preparation for operation while the patient remains in bed, provided the operation can be delayed The combination of rest in bed, restriction of the salt and fluid intake, and adequate amounts of digitalis together with a mercurial diuretic and ammonium chloride will minimize the risk of operating For untreated heart failure the digitalization should be rapid If an emergency operation is necessary and delay is unwise the patient can be given digitalis intravenously and a mercurial diuretic, though this, of course, is not the optimal course. If chest or abdominal taps appear necessary they may be done before the operation to insure minimal pulmonary embarrassment later.

Sedatives

Administration of phenobarbital 0 1 Gm. to 0 2 Gm , pentobarbital 0 1 Gm , or sodium amytal 0 2 Gm. the night before the operation allays apprehension. Sedation should be used with care lest the prolonged effects be additive to those of morphine given pre- and postoperatively.

Chapter 30 Patients with normal hearts may show paroxysmal abnormalities in rhythm under the stress of anesthesia, hypervolemia, and other complications.

EARLY AMBULATION

There has already been enough experience with early ambulation after surgery to indicate that for most patients this is the desirable procedure. There is a general notion that early ambulation *prevents* thrombophlebitis and thromboembolism. A recent analysis does not support this, although it is apparent that convalescence is hastened The effects of mobilization are discussed more fully in Chapter 30.

SUMMARY

It is a matter of record that mortality after surgical procedures is being reduced. Part of this is no doubt due to training and skill, but also in no small part to better preoperative preparation of patients, better technics of anesthesia, and better postoperative care. In a large measure this is due to maintenance of adequate fluid and electrolyte intake and avoidance of the dehydration which follows nausea and vomiting. The introduction of antimicrobial agents has been of great benefit in the treatment of complications caused by infections. Prompt use of oxygen has been beneficial and has lost its morbid implications in the lay mind However, with the increase in use of intravenous fluids complications have often resulted from too vigorous application of this mode of therapy rather than from a defect or weakness on the part of the human organism. I have tried to make the following points. (1) That it is unwise to push fluids too vigorously; (2) that it is more expedient to adapt the quantity of fluids to the individual patient; and (3) that serious harm can be avoided by careful and frequent observation for evidence of overdistention of the circulation with fluid.

Bibliography

The bibliographies for Chapters 29 and 30 are combined at the end of Chapter 30.

INTRAVENOUS FLUIDS

Not every patient requires intravenous fluids while operations are being performed, but this point must be given special consideration when cardiac patients are being operated upon. A patient with a normal cardiovascular system might be able to assimilate the fluids, but in a patient with a damaged heart the extra load may precipitate acute cardiac failure. Even more care should be exercised in patients with a history of congestive heart failure or of diminished cardiac reserve, especially when the history is recent and has necessitated a period of treatment before the operation When fluids must be given during operation attention should be given *to the rate of flow, which may be made so slow that it merely keeps the* infusion system open in case an emergency should require fluids more rapidly or a transfusion should be indicated The use of 5 per cent glucose in cardiac patients *avoids the disadvantage which is inherent in the use of normal saline.*

The intravenous administration of fluids after operation should be gauged by the duration of the operation, the amount of blood lost, the early reactivity, and the functional status of the patient A rule cannot be made about the amounts which may be optimal in all instances, however, very large amounts such as four, five, or six liters a day are rarely needed In many situations 5 per cent glucose in saline may be rapidly enough absorbed when given by hypodermoclysis but would overload the circulation when administered intravenously If fluid is given intravenously the amount in 24 hours should be limited to that absolutely necessary and should be given slowly With a three-way stopcock a venous pressure tube may be incorporated into the infusion system, so that estimations of venous pressure may be made at intervals If this is not possible careful observation for increase in distention of the neck veins should be maintained The lungs should be observed for the appearance of râles Only by extreme care can acute heart failure, acute cor pulmonale, *and angina pectoris from increase in blood volume be avoided*

Because of the possibilities of transfusion reaction and of the appearance of homologous serum jaundice weeks to months later, transfusions should be used *only when they are absolutely necessary*

The venous engorgement and râles in chest, the amount of sweating, and the amount of urine excretion and its concentration are also guides to the replacement of fluid.

Oral administration should replace the intravenous method as soon as possible Many cardiac patients on a limited fluid intake before operation may be given a total of 1800 to 2000 cc in 24 hours on the day of operation and the succeeding day, but this amount should be reduced as soon as possible If the patient has been on a preoperative regimen of mercurial diuretics, digitalis, a low salt diet, and a limited fluid intake one of the mercurial diuretics may be required a day or two after operation and can be resumed even before the remainder of the cardiac schedule The low salt diet should be resumed with the institution of oral feeding Digitalis may be given intravenously without interruption of the schedule and the dosage may be adjusted as necessary. If acute heart failure with pulmonary edema should arise in a patient who has been on a cardiac regimen up to time of operation, intra-

Digitalization

Patients should not be digitalized before operations unless there are definite indications, cardiac insufficiency and appropriate arrhythmias. So-called "prophylactic" digitalization of patients before operation may be harmful Digitalis decreases the cardiac output of the normally functioning heart and reduces its size (Stewart and others), effects which are undesirable when the cardiovascular system must adjust to the requirements of anesthesia and the operative procedure If there is adequate time in patients exhibiting auricular fibrillation the ventricular rate should be slowed satisfactorily with digitalis before operation is undertaken It has already been emphasized that patients suffering from congestive heart failure should be digitalized and should attain as satisfactory a state of compensation as is compatible with the time available

Nitroglycerin

Nitroglycerin may be given to patients with angina pectoris in order to prevent pain which may otherwise result from apprehension

CHOICE OF ANESTHETIC

Local anesthesia may be the safest measure if it is appropriate and the patient is of the temperament adaptable to this method. It is especially suitable for patients with Graves' disease who have been satisfactorily prepared by the use of iodine and propylthiouracil but require thyroidectomy However, ether and oxygen also provide satisfactory anesthesia for cardiac patients When rebreathing is carried out afterward with 100 per cent oxygen, and penicillin is used, the pulmonary complications can be minimized. Spinal anesthesia should be used with care because the blood pressure may fall, even though paredrine and neosynephrine may be given to prevent this However, the maintenance of the optimal level of blood pressure cannot be guaranteed A later rise in blood pressure might result when the heart could least afford this load Spinal anesthesia may also be contraindicated in certain patients suffering from arterial hypertension and from coronary artery disease Fall in blood pressure in hypertensive patients may result in cerebral thrombosis, coronary thrombosis, or myocardial infarction without thrombosis; in patients with coronary artery disease it may result in coronary thrombosis or myocardial infarction without thrombosis For certain operations, for instance those relating to the urinary bladder, a low spinal anesthesia would not be expected to cause a fall in blood pressure and might therefore be the anesthetic of choice

Cyclopropane with oxygen and curare is a very satisfactory anesthetic for many noncardiac patients This is especially true in gastrointestinal surgery, where nausea occurs less frequently with cyclopropane and oxygen than after other general anesthetics On the other hand, the tendency of cyclopropane to induce cardiac irregularities such as premature contractions, ventricular paroxysmal tachycardia, and ventricular fibrillation makes the selection of this anesthetic for cardiac patients unwise. In certain instances pentothal sodium administered intravenously may be recommended.

Alkalosis

One-sixth molar sodium lactate given intravenously to prevent crystalluria when sulfadiazine is given alone or together with gastric suction, as well as alkaline powders in the treatment of peptic ulcer, may lead to alkalosis (Grace and Barr), particularly in patients with emphysema. Mental aberration, delirium, epileptiform seizures, and disorientation may occur. Respirations become shallow and slow. There may be muscle twitchings and evidences of tetany, such as carpopedal spasm, and Chvostek's and Trousseau's signs The urine output falls and the urine shows evidences of renal damage. At this time the carbon dioxide combining power of the blood may be greatly increased, the serum chlorides may be decreased, and there may be hypocalcemia and rise in blood urea nitrogen. Electrocardiograms may point to hypocalcemia and disturbances in electrolyte balance before the clinical condition of the patient directs attention to the alkalotic state (Fig 68).

The prompt use of ammonium chloride by mouth—or by the intravenous route, if there is more urgency—and of sodium chloride rectifies the alkalosis. Clearing of the abnormal mental, neurologic, and electrocardiographic signs follows.

Ammonium chloride is given as a 2 per cent solution in distilled water after being autoclaved One liter of the solution, equivalent to 20 Gm ammonium chloride, is given over a period of two and one-half to three hours Venous distention is guarded against Evidence of renal insufficiency may persist for varying intervals afterward, perhaps for many months. The damage may be permanent.

ELECTIVE SURGERY

It is better to operate on a patient with organic heart disease who has a lesion amenable to surgical treatment at a time which can be chosen by the surgeon when the patient is in the best state possible, than to wait until an emergency operation is required.

For example it is more expedient to operate on a cardiac patient who has gallbladder disease with attacks of gallstone colic in a free interval than to have to operate as an emergency measure Even a history of myocardial infarctions need not be a contraindication to removal of the gallbladder if there is careful preoperative preparation and skillful surgery Patients suffering from angina pectoris and gallbladder disease may experience amelioration of the anginal symptoms after cholecystectomy A similar point of view about elective surgery applies to other surgical diseases such as hernias which may strangulate. When emergency surgical intervention is required in cardiac patients, the blending of all the skills of the internist, the anesthetist, and the surgeon is required to provide the best regimen.

SURGERY IN THE DIFFERENT TYPES OF HEART DISEASE

In all the categories of heart disease the risk of surgery can be greatly reduced by individualization of the treatment and by careful supervision of the postoperative management.

Patients who suffer from *congenital heart disease without cyanosis* may not

venous aminophyllin 0.24 to 0.48 Gm. should be given slowly at once together with an injection of a mercurial diuretic. Oxygen is provided if it is not already being used.

Blood Plasma

When the serum proteins are low or when shock occurs, plasma may be required. However, blood plasma may increase the load on the circulation and in addition *may cause homologous serum jaundice later.*

Fluids by Hypodermoclysis

When cardiac patients, especially those with coronary thrombosis or heart failure, cannot take fluids orally they may be given by hypodermoclysis subcutaneously Normal saline and 5 per cent glucose may be used Hyaluronidase may be added to the solution to hasten its absorption from the subcutaneous tissues. If supplemental fluids have to be kept up for long periods and there is loss of fluid by suction or in vomitus, restoration of potassium by the addition of its chloride to the solution may be required. In patients in whom heart failure is of concern the sodium intake must be watched.

OXYGEN

The use of oxygen prophylactically for 24 hours or longer after operation may be of benefit for most cardiac patients It is worth the added expense by insuring a smoother convalescence

PENICILLIN

Penicillin or other antimicrobial agents should be used after operation when there is any question of infection or of postoperative pulmonary complications. Patients should be kept comfortable by the proper use of hypnotics and sedatives during convalescence, but frequent deep breathing and turning of the patient are essential for the prevention of pulmonary complications.

DISTURBANCES IN ELECTROLYTE BALANCE

Sodium and Potassium

The administration of sodium lactate to prevent crystalluria when sulfonamide drugs are given, as well as sodium bicarbonate and sodium chloride, may lead to the retention of sodium ions. Storage of body fluid may precipitate acute cor pulmonale or acute heart failure with pulmonary edema Potassium bicarbonate as a substitute for sodium bicarbonate is not recommended; if there is decrease in renal function, the potassium ion may not be excreted adequately and may accumulate sufficiently to produce toxic effects on the heart muscle Auricular standstill, defects in intraventricular conduction, and bizarre ventricular rhythms have been recorded by *Stewart, Shepard, and Horger. Death may* result. When there is loss of sodium or potassium careful restitution should be made (Chapter 31).

vision of the administration of fluids, and prompt utilization of cardiac drugs are necessary.

Patients with *auricular fibrillation* need present no unusual problems during operation because of the auricular fibrillation per se, provided the ventricular rate is adequately retarded with digitalis before and after operation and the patient is free of failure. Embolic phenomena are no more likely to occur for the first time in these patients than in those with normal rhythm. Attempts to convert the rhythm to normal mechanism should not be made. Added amounts of digitalis may be required to slow the ventricular rate if it rises during fever.

It has already been pointed out that patients suffering from Graves' disease who have had heart failure even in the presence of auricular fibrillation can be safely carried through thyroidectomy. Restoration of cardiac compensation by the use of digitalis, a low salt diet, restriction of fluids, and mercurial diuretics together with the administration of iodine and propylthiouracil to lower the basal metabolic rate are required first. Attempt should not be made to restore normal sinus rhythm with quinidine before thyroidectomy. A two-stage operation under local anesthesia may be the procedure of choice for some of these patients. Ether and oxygen may be used in those requiring general anesthesia.

Diabetic patients are prone to the early development of arteriosclerotic changes which may be present in the coronary arteries in addition to the easily detected alterations of the peripheral vessels. These patients should be adequately prepared before operation and the insulin dosage carefully regulated. Insulin should best not be given immediately before operation, a marked fall in blood sugar with hypoglycemia may give rise to acute myocardial infarction. Shock and fall in blood pressure from any cause, especially anesthesia, should be avoided, since they predispose to coronary thrombosis. The fluid intake, when infusions of glucose are required, should be balanced against the functional capacity of the heart.

Paroxysmal cardiac rhythms during operation rarely constitute serious crises but should be met with immediate and appropriate measures. A discussion of rhythms occurring under anesthesia and the possibility of using procaine derivatives intravenously will be found in Chapter 5. If electrocardiographic machines are available in the operating room so that the nature of the rhythm can be determined, a digitalis preparation may be given intravenously when necessary as in auricular fibrillation, auricular flutter, and supraventricular paroxysmal tachycardias. Pronestyl might be used intravenously when auriculoventricular or ventricular paroxysmal tachycardia is recorded. Quinidine lactate is available for intravenous administration but its use is not recommended. Procaine amide hydrochloride (pronestyl) may find application in the treatment of not only the ventricular and auriculoventricular paroxysmal tachycardias but also of other paroxysmal rhythms occurring during operation (p. 178). Paroxysmal rhythms and other abnormal rhythms occurring postoperatively are treated as in other circumstances.

EARLY AMBULATION

Early ambulation after surgical procedures is now accepted as a part of the regimen of most patients. Convalescence of patients who were in good general health beforehand is no doubt shortened by early ambulation. This course may

experience any special difficulties during surgical procedures (see Chapter 6). When consideration is given to the magnitude of the Blalock-Taussig operation in patients with the tetralogy of Fallot, the extent of operative procedures that can be carried out is impressive when surgical skill and precision in preoperative and postoperative care are combined.

The surgical treatment, anesthesia, and management of patients subjected to pericardiectomy for *chronic constrictive pericarditis* are given at length in Chapter 21, as a special example of the cooperative effort of surgeon and internist.

The risks of operating on patients with hypertension may be lessened by avoiding the use of anesthetics which cause a fall in blood pressure. This lessens to some extent the hazards of cerebral accidents and myocardial infarctions The management of patients undergoing operation of *thoracolumbar sympathectomy for hypertension* has been described in Chapter 9.

The management of patients subjected to surgical procedures for the relief of *angina pectoris* has been described in Chapter 12

Patients with *rheumatic heart disease* but without heart failure need not present any unusual risks during surgical procedures if adequate care is exercised. The hazards are increased after the onset of auricular fibrillation and of failure Nevertheless, even with these unfavorable complications patients may tolerate satisfactorily even prolonged operations such as radical mastectomy and thyroidectomy

Patients suffering from arteriosclerotic heart disease present more risks during surgical operation than do those with rheumatic heart disease. The presence of abnormal rhythms and of diminished renal function are unfavorable factors

Not infrequently I have been presented with the problem of a patient who has sustained recent coronary thrombosis, perhaps within a matter of weeks, and is found to have a carcinoma of the stomach which is thought especially amenable to cure if completely removed Account is taken of the severity of the myocardial infarction, the progression of electrocardiographic changes, the sedimentation rate, and the general state of the patient It may be appropriate to decide that operation should be undertaken within four to eight weeks after the onset of the myocardial infarction.

Patients with *syphilitic heart disease* may present more risks in surgery than those with rheumatic heart disease, but fewer than those with arteriosclerotic heart disease.

Bundle branch block, except the wide S wave type, usually implies serious myocardial damage On the other hand the cardiac function may not be compromised by routine demands. Of course, if the operation is necessary, the risks must be taken. If the operation is an elective one for a lesion or a disease which may not require correction for an indefinite period, the balance should be struck between the probable life expectancy in the presence of bundle branch block and the life expectancy if the patient were freed of the disease for which the surgery is contemplated.

Bundle branch block of the S wave type carries with it an essentially normal life expectancy. I have approved surgical operations on many patients with the usual forms of bundle branch block—even those in whom the bundle branch block resulted from myocardial infarction—when the gain that might be derived outweighed the risk of the cardiac status. Careful selection of anesthetic, wise super-

stasis and atelectasis. Atropine sulfate in amounts sufficient to retard bronchial secretions may cause an undesirable increase in heart rate. Paredrine in 10-mg. doses may be given intramuscularly in the treatment of peripheral vasomotor collapse, and in the prevention of fall in blood pressure after spinal anesthesia. This drug does not increase the cardiac output as ephedrine does. One hundred per cent oxygen is used in rebreathing after anesthesia instead of carbon dioxide.

The treatment of *thrombophlebitis* has been described in Chapter 4. When pulmonary infarction occurs, anticoagulants may be indicated. Electrocardiograms may be useful in the diagnosis of this accident.

Re-expansion of an atelectatic lobe or of a collapsed lung may be facilitated by having the patient breathe 100 per cent oxygen and by bronchial aspiration of mucus. The patient should be encouraged to cough and to expectorate the mucus. If his condition warrants this amount of manipulation, it may be appropriate to use the bronchoscope so that aspiration of a plug of mucus can be carried out under direct vision The position of the patient should be changed frequently. If there is pleuritic pain associated with the atelectasis, and if sedation and morphine are contraindicated because depression of respirations is undesirable, local nerve block may allow free respiratory movements without pain.

Pleural Fluid and Pneumothorax

When surgery of the chest and the heart is carried out, accumulations of bloody fluid and air in the pleural cavity may occur, alone or together, and with atelectasis. Should amounts sufficient to embarrass respiration accumulate, the air or fluid can be removed by tap. Frequent roentgenograms of the chest may be required to verify the diagnosis and to discover whether progress is favorable. Expected deviations of the trachea to the side of atelectasis may be nullified by pneumothorax. When there is a moderate amount of free air in the pleural cavity, this amount might appear to increase not only on physical examination but also in roentgenograms. This is caused by an accumulation of fluid forcing the air into an area where more prominent signs can be detected and occurs particularly when air rises to the apex of the pleural cavity upon the patient's sitting up

SUMMARY

For the most part patients with heart disease tolerate a remarkable amount of surgical manipulation of the heart in the treatment of intrinsic heart disease. In addition most patients with organic heart disease tolerate anesthesia and the surgical manipulations which are required in the treatment of surgical complications or of primary diseases. When each individual patient is treated with special care with respect to preoperative preparation, skillful anesthesia and management during operation, careful and skillful surgery, and close and individual supervision of the postoperative care by physicians and nurses, the results are amazingly good. This is a more satisfactory approach than following an over-all regimen for treating all of these patients. With the present increase in life span and with the prospect of an even greater percentage of the population suffering from these affections of the

make the patient very uncomfortable during the first few days; indeed, for many patients ambulation the next day or for many days afterward is not possible.

Patients suffering from organic heart disease and those without histories of congestive heart failure, as well as those who may have had heart failure in the past but are well compensated at the time—these too may well have their convalescence hastened by early ambulation if careful observation is maintained. On the other hand, patients who have evidence of congestive heart failure should not be mobilized faster than the state of the compensation warrants. Patients remaining in bed should be turned frequently, should be instructed to take frequent deep breaths, and should move their legs freely, in order to prevent pulmonary and peripheral stasis This regimen also tends to prevent thrombophlebitis, thromboembolism, pulmonary infarction, hypostatic pneumonia, and the weakness which follows bed rest Postoperative complications such as hemorrhagic pleural effusion, atelectasis, and pneumothorax in patients who have had chest surgery delay the institution of early ambulation

Deitrick, Whedon, and Shorr have shown certain alterations in the metabolism of patients who are immobilized by casts for six to seven weeks. Several weeks may be required after mobilization for recovery to normal levels There were no significant changes in the mechanism of blood coagulation, in circulation time, in heart size, in electrocardiograms, in blood pressure, in hematocrit, in blood count, or in vital capacity. Immobilization resulted in decline in the mechanisms brought into play in maintaining an adequate circulation in the erect position, as exhibited by increase in tendency to faint when patients were subjected to tests on a tilt table

In such patients, as we have said, there was rigid immobilization These results would not apply to patients who are free to move around in bed They would apply more precisely to patients with fractures who required immobilization or to patients with detached retinae, for whom absolute quiet for a period of time may be necessary.

TREATMENT OF COMPLICATIONS

Skillful preoperative and postoperative care decreases the number of complications. This involves care with respect to state of compensation before and after operation, a short period of anesthesia, the avoidance of deep sedation, avoidance of overloading the circulation with fluids, use of a catheter to remove bronchial secretion, rebreathing of 100 per cent oxygen, frequent changes in position of the patient, frequent deep breathing exercises after the patient reacts, and the avoidance of limitation of respiratory movement by tight chest or abdominal binders. Avoidance of intestinal distention by rectal tube and turpentine stupes may prevent restriction of respiratory function.

Pituitrin and pitressin should be used with care in the treatment of abdominal distention, because of their vasoconstricting properties they may induce angina pectoris. The administration of ergot after gynecologic procedures also may induce attacks of angina pectoris. Epinephrine too may lead to angina pectoris and to untoward effects in patients with coronary artery disease. Morphine should be used with care because it decreases the depth of respirations and may promote pulmonary

CHAPTER 31

Effect of Electrolyte Changes in Blood on Heart and Circulation

Physiologic data have been available for many years which reflect the importance of a carefully controlled chemical medium for maximal efficiency in the operation of the cardiovascular system This constancy of the internal environment was emphasized by Claude Bernard Alterations in function with changes in sodium, potassium, and calcium content of the bathing solution or with change in pH and in pCO_2 have been demonstrated in basic physiologic laboratory experiments. Clinical recognition of these alterations awaited the simplicity of the flame photometer and other improved analytic procedures. Newer methods are also now available for the estimation of acid-base balance It is probable that the recent emphasis on electrolyte and fluid abnormalities in heart failure will stimulate further correlations of chemical pathologic physiology with clinical states

A large body of literature has accumulated on empirical electrocardiographic changes in various states not of primary cardiac origin: in diabetic acidosis, in gastric alkalosis, in familial periodic paralysis, in nephritis, in Addison's disease, and in many other states in which hypopotassemia, hyperpotassemia, hypocalcemia, and alkalosis are known to occur More recently metabolic studies have been accomplished demonstrating the relationships between changes in these variables and in the electrocardiograph patterns. But the presence of electrocardiographic changes do not necessarily imply a change in functional capacity. Clinical observations are needed to determine the effect of the sublethal chemical abnormalities on functional capacity. An attempt will be made here to relate certain of the observations on chemical abnormalities to the cardiovascular system.

heart and vascular system characteristic of the older age group, it is of moment for physicians to increase their skill in the management of these patients when they require surgical treatment.

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Electrocardiograms and Blood Chemistry and Urine Data of a Woman 46 Years of Age with Diabetic Acidosis

A was taken on November 26, 1948, when patient was in diabetic acidosis Q-T time was 0 35 second with a heart rate of 95—within the upper limits of normal CO_2 combining power was 26 volumes per 100 cc, blood sugar 388 mg per 100 cc, urine gave a 4+ reaction for sugar and a 1+ reaction for acetone.

B was taken the following day when CO_2 combining power was 41 volumes per 100 cc, blood sugar 172 mg per 100 cc, urine gave a 0 to 2+ reaction for sugar and was negative for acetone T waves have decreased in amplitude and have become negative in three standard leads Q-T time was 0 40 second with a heart rate of 98 per minute, the upper limit of normal being 0 35 second

C, taken November 28, shows *T* waves have undergone further changes and have become upright in *Leads I, II,* and *IV*. Following day laboratory data were as follows CO_2 combining power 58 volumes per 100 cc, blood sugar 346 mg per 100 cc., urine sugar 3+, and urine negative for acetone Q T time was now 0 38 second, with heart rate 88 per minute, upper limits of normal being 0 37 second

D, taken December 3, showed slight changes in T waves. Laboratory data December 2, 1948 were as follows CO_2 combining power 58 volumes per 100 cc, blood sugar 441 mg. per 100 cc, urine sugar 4+, and urine negative for acetone December 3 serum potassium was 4 4 mEq/L. On December 4, serum calcium was 7 9 mg per 100 cc. Q-T time was now 0 38 second, the upper limit of normal being 0.35 second.

E, taken December 9, showed normal configuration of electrocardiogram except for left axis deviation Q T time was 0 37 second, now within upper limits of normal, heart rate being 78 per minute Laboratory data were as follows: CO_2 combining power 64 volumes per 100 cc, blood sugar 322 mg per 100 cc, urine sugar 3+, urine negative for acetone.

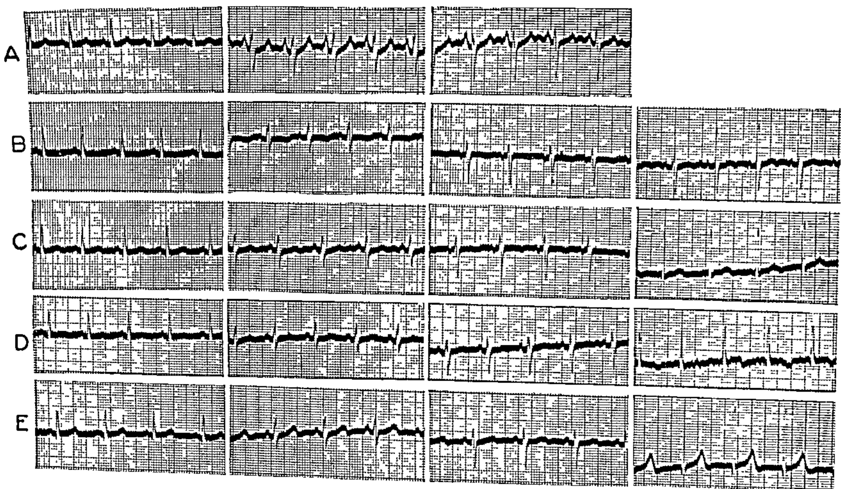


Fig 61.

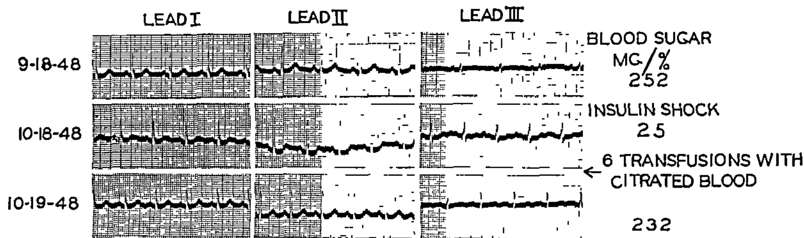


Fig 62

Electrocardiographic Changes which Accompanied Insulin Shock in a Woman 62 Years of Age

Patient had diabetes and had recent hemorrhages from esophageal varices First electrocardiogram was taken September 14, 1948, when blood sugar was 252 mg per 100 cc Electrocardiogram taken October 18 was taken during insulin shock at a time when blood sugar was 25 mg per 100 cc There have been alterations in form of T waves and lowering of RS T segments Following this record patient had six transfusions each of 500 cc citrated blood. Electrocardiogram on October 19, at a time when blood sugar was 232 mg per 100 cc, shows reversion to the configuration prevailing September 14

ELECTROLYTE CHANGES IN SPECIFIC CIRCUMSTANCES

Diabetic Acidosis and Administration of Insulin

Clinical Manifestations

There may be profound weakness in patients with diabetic acidosis about 24 hours after the beginning of effective treatment, as well as in patients who have vomited a great deal. It is recalled that potassium is lost in the vomitus and in the urine as base. In some instances the symptoms may be as marked as in patients with familial periodic paralysis (p. 526). In patients with diabetic acidosis, the administration of potassium by the oral or intravenous route results in disappearance of all signs and symptoms of hypopotassemia

Electrocardiographic Signs

In diabetic acidosis with dehydration and vomiting electrocardiograms may show profound changes which can be attributed to electrolyte changes in the blood. The serum potassium is normal or elevated before therapy and falls to concentrations below normal soon after the institution of treatment which makes use of hydration, insulin, and glucose When the serum potassium is elevated the T waves in the electrocardiogram are tall with a narrow base and when the value is below normal the height of the T waves is diminished or inverted, and the Q-T interval is prolonged In short there is a correlation between decreased amplitude of T waves and low serum potassium levels.

Bellet and Dyer have also found reversible changes to be shown in electrocardiograms of patients suffering from diabetic acidosis. These alterations, characterized by lengthening of Q-T interval, depression of RS-T segments, and inversion of T waves, occurred about 24 hours after insulin therapy had been started, at a time when the acidotic state had been relieved by appropriate therapy. Martin and Wertman found that 43 per cent of their patients with diabetic acidosis who exhibited prolonged Q-T intervals showed a low serum potassium or calcium Further discussion of the correlation of hypopotassemia and electrocardiographic changes is to be found on p 524 Figure 61 shows a series of electrocardiograms which record the changes observed in a patient during diabetic acidosis.

The configuration of the electrocardiogram showing prolongation of the Q-T interval due to hypocalcemia differs from that due to hypopotassemia. In the former the RS-T segment is isoelectric and shows a long interval before the upward or downward stroke of the T wave The T waves are very precise (Figs. 61 and 67) In the latter the S wave shows a sluggish swing up into the T wave, the RS-T segment showing deviation, and the T wave may show several undulations.

The electrocardiogram may show marked alterations during insulin shock with hypoglycemia There may be depression of the RS-T segments and negativity of the T waves as in Figure 62. The same figure also shows prompt reversal to the original configuration with recovery from shock and restoration of the level of blood sugar.

the hemoconcentration, the reduction in plasma volume, in the sodium and chloride concentrations of the serum and in the blood sugar, and the concentration of serum potassium are more marked.

Patients who are being maintained on ration doses of *desoxycorticosterone acetate* require close supervision and careful observation of the salt intake because of the sodium and chloride retention which this drug encourages. Moreover maintenance of a high carbohydrate intake is essential for the prevention of hypoglycemia. Sodium retention provokes the retention of water, which leads to increase in blood volume. There may be increase in body weight, the blood pressure rises to hypertensive levels, edema appears, the heart dilates, and signs and symptoms of pulmonary edema may become apparent. Prompt reduction of the dose of the drug with the first evidence of rapid gain in weight or appearance of edema may prevent more serious consequences.

Electrocardiographic Signs

In chronic adrenal insufficiency (Addison's disease) and in Addisonian crises marked changes in the electrocardiogram may occur, which reflect alterations in the electrolyte pattern of the blood. There may be changes in the T waves and RS-T segments: lowering of the amplitude of the T waves and alterations of their contour (Fig 63). The changes may be marked but they are not specific. They are the result of the summated effect of the several changes in the constituents of the blood on the heart muscle: reduction in concentration of sodium ions, increase in concentration of potassium ions, and hypoglycemia With the use of normal saline and glucose intravenously, of adrenal cortical extract, and of desoxycorticosterone acetate and perhaps transfusions, the electrocardiographic aberrations disappear.

Hyperpotassemia

Electrocardiographic and Clinical Manifestations

Potassium salts have found a wide use in the treatment of various manifestations of heart disease For instance, potassium chloride has been used as a diuretic agent in heart failure Potassium iodide until recently has been considered a component of the treatment of syphilitic heart disease; it has been given to eliminate premature contractions. The same drug has been recommended for the treatment of arteriosclerosis Potassium acetate has been used as a diuretic in the treatment of nephrosis Recently potassium bicarbonate has been recommended as a substitute for sodium bicarbonate in patients with heart failure, in order to prevent crystalluria when sulfonamide drugs are given.

However, potassium in increased amounts in the circulating blood acts as a poison on cardiac tissue, it decreases the activity of the sinus node, leading to cessation of its activity and to auricular standstill, it also hinders the conduction of the excitation through the ventricular muscle so that the QRS conduction time is prolonged The net result of these two effects in extreme instances of potassium poisoning is cessation of auricular activity with the onset of bizarre ventricular rhythms which are incapable of maintaining an adequate circulation. Death with cardiac standstill in diastole follows unless restoration of normal cardiac activity is accomplished promptly. Symptoms from less severe grades of intoxication from

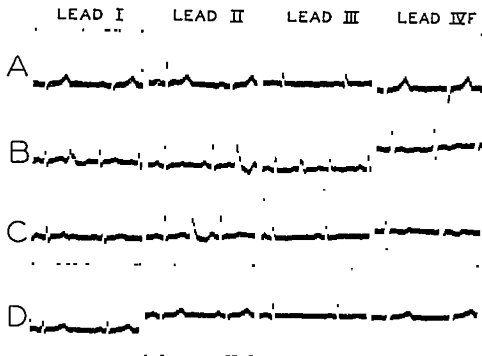


Fig 63

Electrocardiographic Changes in a Man 40 Years of Age Suffering from Addison's Disease

Patient had been under observation at New York Hospital for five years He was admitted July 5, 1948 because of vague pains in chest associated with respiratory infection of eight days' duration There was fever

A, taken on June 2, 1947, served as a control Configuration was essentially normal

B, taken July 5, 1948, showed T_1 had decreased in amplitude, T_2 become diphasic and decreased in amplitude, T_3 negative and coved, and T_4 negative and coved Q-T time was prolonged

Frequent interpolated right ven-

was 19.3 mg per 100 cc. (4 9

nal cortical extract intravenously,

and desoxycorticosterone acetate and penicillin intramuscularly, patient improved.

C, taken July 7, 1948, showed that T_1 had increased in amplitude, T_2 was now upright, T_3 was less negative, and T_4 had increased in amplitude, was no longer coved, and was less negative. Interpolated premature contractions still occurred. At this time serum potassium was 14 0 mg

mEq/L)

T waves were upright in all leads,

e control configuration of June 2,

1947

Addison's Disease

Clinical Manifestations

Patients with Addison's disease usually have hypotension and small hearts. These are due to the loss of sodium and chloride from the body and reduction in plasma volume. There is hemoconcentration, low basal metabolic rate, and hypoglycemia. Patients with Addison's disease may exhibit crises as a result of intercurrent infection and of periods of stress, strain, and overexertion. At such times

potassium iodide include sinus tachycardia, supraventricular paroxysmal tachycardia, complete auriculoventricular dissociation with rapid irregular ventricular sequence, and progressive first-degree heart block. Decrease in amplitude of the T waves with diphasic components and negativity, and configurations even suggesting myocardial infarction may be recorded. It is recalled that increase in serum potassium usually causes increase in amplitude of T waves It is apparent therefore that the use of potassium salts is not without danger.

If there is renal insufficiency two difficulties may arise: (1) The kidneys may not be able to excrete the increased amount of potassium given as a therapeutic agent, the serum potassium rises and toxic effects may result (2) On the other hand, if the renal function is impaired the kidneys may not be able to excrete normal amounts of potassium. As a consequence, without the ingestion of added amounts of this ion and only from the amount available in the body and in the diet, the serum potassium rises beyond normal levels, so that it may attain proportions which are harmful to the heart. Toxic manifestations appear.

Stewart and Smith have demonstrated in electrocardiograms the toxic effects of potassium when potassium salts are used in the ordinary amounts in the treatment of syphilis They have also recorded death from the use of potassium chloride as a diuretic in heart failure, in this instance there was auricular standstill and a bizarre ventricular rhythm with bundle branch block (Fig 21). Stewart, Shepard, and *Horger have reported examples illustrating both spontaneous potassium intoxication* and that resulting from increased administration of the ion They recorded auricular standstill with a bizarre ventricular rhythm (Fig 64) resulting from the use of potassium bicarbonate as a substitute for sodium bicarbonate during the administration of sulfadiazine Recovery took place after discontinuance of potassium bicar*bonate, since the kidneys were able to excrete the excess The second example was of*

spontaneous

f intravenous

hours later

In both these patients almost identical electrocardiograms were recorded when *the potassium content of the blood was around 10 mEq per liter*

Observations have shown that the use of normal saline and 5 per cent glucose promptly by the intravenous route have been effective in causing a rapid fall in serum potassium A cationic exchange resin (without potassium) may be useful in lowering the serum potassium It may be that around 10 mEq per liter of potassium *is the level at which toxic effects on the myocardium are objectively apparent.* From Tarail's careful observations in a number of patients suffering from renal insufficiency, electrocardiographic abnormalities occurred in certain instances when the range of serum potassium was between 6 8 to 7 6 mEq. per liter but were consistently present at concentrations greater than 7.8 mEq per liter.

I have recently had occasion to see a patient with profound cardiovascular changes which may have been related to the increased level of potassium in the blood This patient, a man 47 years of age, had anuria following several days of continuous vomiting An adequate history could not be obtained at the time of his admission to hospital Because the blood pressure was elevated it was at first thought that the patient suffered from uremia. The urine volume was only a few cubic

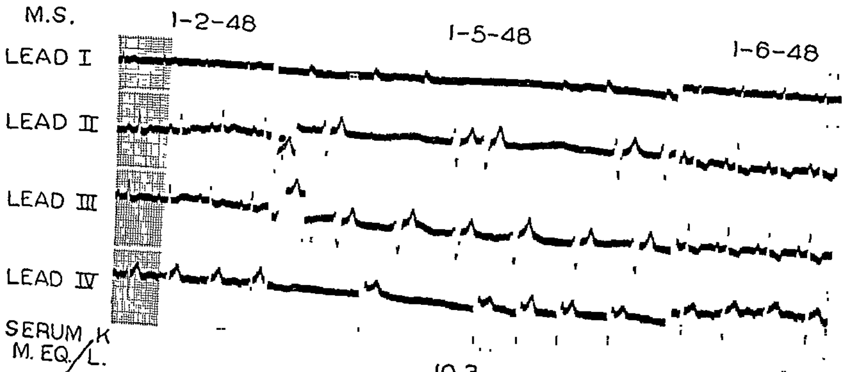


Fig 64

Electrocardiographic Changes in a Man 72 Years of Age, who Exhibited Cardiac Arrhythmia as a Consequence of Potassium Intoxication when Potassium Bicarbonate was Given in Conjunction with Sulfadiazine.

A, taken January 2, 1948, showed normal sinus rhythm

B was taken January 5 after administration of potassium bicarbonate 20.0 Gm in 48 hours Potassium bicarbonate substituted for sodium bicarbonate as an alkalizing agent during administration of sulfadiazine because patient had bronchopneumonia, and had recently recovered from cardiac decompensation. In this record there was auricular standstill Heart beat was irregular as a consequence of stimuli rising from a focus in right ventricle QRS complexes were deformed and conduction time was prolonged to 0.15 second Serum potassium level at this time was 10 mEq/L, and serum sodium 128 mEq/L. Potassium bicarbonate was discontinued after this record was taken and the following day normal sinus rhythm had been restored Serum potassium at this time had fallen to 5.9 mEq/L, normal values being considered to lie between 3.9 and 5 mEq/L. Serum sodium was unchanged

C was taken on January 6, 18 hours after potassium had been discontinued

In this patient administration of a potassium salt in presence of moderate decrease in renal function resulted in an elevation of serum potassium to toxic levels and initiation of auricular standstill and a ventricular rhythm With discontinuance of potassium salt kidneys were able to excrete excess potassium, which fell to approximately normal levels within 18 hours, and heart rhythm reverted to normal sinus rhythm (Stewart, H J, Shepard, E M, and Horger, E. L. Electrocardiographic manifestations of potassium intoxication. Am J. Med 5:821, 1948)

Electrocardiographic Changes in a Man 47 Years of Age

Patient suffered from acute renal failure—*syndrome of lower nephron nephrosis. Electrocardiograms show effect of multiple electrolyte aberrations* hypocalcemia, low sodium, and hyperpotassemia

Patient was admitted to hospital with uremia, having vomited for some while before admission Since blood pressure was elevated it was at first the opinion that he had *hypertension with uremia After patient had been under observation for 24 hours* it became apparent that he was suffering from loss of sodium chloride and that he had a lower nephron nephrosis

Electrocardiogram, taken January 21, 1949 at 10 50 A M, showed left bundle branch block. The QRS time was 0 20 second The *form of the QRS complexes suggested that conduction defect may have been due to hyperpotassemia* although serum potassium was only 5 8 mEq/L The day before, January 20, serum sodium was 121 mEq/L.

Electrocardiogram taken January 22, 1949 at 10 40 A M showed normal sinus rhythm with persistence of bundle branch block *Amplitude of QRS complexes in three standard leads had decreased*

Electrocardiogram taken at 2 30 P M the same day showed occasional P waves with irregularity of the ventricular complexes, a rhythm which suggested more strongly hyperpotassemic effects. Slurring of S wave as it merged with T wave, however, suggested hypo *potassemia*

Electrocardiogram taken at 3 00 P M, showed that regularity had been restored to the ventricular sequence and P waves appeared in front of all QRS complexes At 4 30 P M, on this day potassium had risen to 8 2 mEq/L At this time 300 cc of 5 per cent saline was given intravenously (15 Gm sodium chloride) because of low sodium content of serum, 125 mEq/L

At 10 15 P M, that is six hours after administration of hypertonic saline intravenously, and before the appearance of clinical pulmonary edema, another electrocardiogram was taken It showed that configuration of QRS complexes had changed QRS time had decreased to 0.14 second Bundle branch block was present but configuration indicated a defect in right branch

It was our impression at that time that the appearance of S_1 and S_2 indicated the effects of right ventricular strain and it was suggested that pulmonary edema might appear Blood samples taken at 1 00 A M on January 23 after the infusion showed that serum potassium remained at 8 0 mEq/L and serum sodium was now 133 mEq/L Electrocardiogram taken at 8 00 P M showed QRS conduction defect had disappeared QRS time was now 0 09 second Right axis deviation remained There were typical signs of frank pulmonary edema

Electrocardiogram taken January 24, after the signs of the pulmonary edema had disappeared, showed right axis deviation was still present QRS time was normal Serum potassium was 6 4 mEq/L and sodium 142 mEq/L.

LEAD I LEAD II LEAD III LEAD IV $K_{M./E./Q.}$ $NA_{M./E./Q}$

1-21-49
10 50 A.M.
5.8 (1-20-49) 121

1-22-49
10:40 A.M.

2.30 P M.

3 00 P.M.
8.2 (4·30 P.M) 125

300 CC. 5 PER CENT SALINE INTRAVENOUSLY (15 GM. NACL)

10 15 P M.
(6 HRS. AFTER SALINE)
BEFORE CLINICAL PULMONARY EDEMA
8.0 (1 00 A.M.) 133

1-23-49
8 00 P.M.

1-24-49
6.4 142

Fig. 61

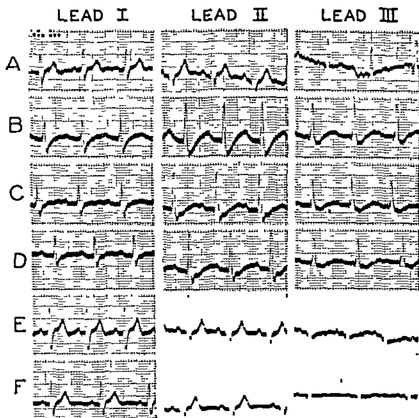


Fig 66

Electrocardiographic Changes in a Man 19 Years of Age who Suffered from Familial Periodic Paralysis

A, taken February 14, 1936, serving as a control, was essentially normal

B was taken June 18, 1939 during an attack of paralysis Paralysis had been present for three days Only voluntary movement patient could make below level of the neck was slight motion of thumbs and index fingers Speech was slurred Q T time was prolonged, as well as P R and QRS times RS T was slurred Serum potassium at this time was 11 mg per 100 cc (half the normal value), serum calcium 10 7 mg per 100 cc

C was taken 85 minutes after administration of first dose of 4 2 Gm of potassium chloride Q T time remained prolonged as did P R time QRS complex showed less deformity and S waves were less split and showed less delay in reaching the isoelectric line At this time serum potassium remained at 11 mg per 100 cc

D was taken 110 minutes after second dose of 4 2 Gm of potassium chloride Q-T time remained prolonged, QRS time was 0 11 second Splitting of S waves was less marked Delay in return to isoelectric line was not so pronounced Serum potassium was 12 1 mg per 100 cc

Within a few hours there was dramatic improvement with recovery from paralysis E was taken on June 19, 1939, and was in all essential details similar to the control (A) Q T time was within normal limits Serum potassium was 25 3 mg per 100 cc—that is to say a high normal level—serum calcium 11 1 mg per 100 cc

F was taken October 24, 1939, approximately four months after E It was essentially like A and E Patient had suffered no further attacks Serum potassium was 18 mg per 100 cc at this time, serum calcium 11 7 mg per 100 cc (Stewart, H J, Smith, J J, and Milhorat, A. T.: Electrocardiographic and serum potassium changes in familial periodic paralysis Am J. M. Sc 199 789, 1940)

centimeters in 24 hours although the fluid intake was adequate. On the sixth day after admission the electrocardiogram showed the pattern of left bundle branch block (Fig. 65), the configuration suggesting a high level of serum potassium. The sodium was found to be low, 125 mEq/L., the potassium high, 8.2 mEq/L., and the chlorides low, 80 mEq L. At this point it was thought that the patient had acute renal failure or the lower nephron nephrosis syndrome, and intravenous hypertonic saline was given. Three hundred cubic centimeters of a 5 per cent solution was given, that is to say 15 Gm. sodium chloride Within six hours left bundle branch block disappeared, and was replaced by right bundle branch block, the QRS time being 0.14 sec. (Fig. 65). It was postulated that the right axis deviation with splitting of the S waves pointed to an acute cor pulmonale, indicating acute pulmonary hypertension. Within a few hours the patient went into frank pulmonary edema, requiring digitalis and oxygen. At the time of the change in site of the bundle branch block the potassium level in the blood had not decreased, nor had the sodium and chloride levels risen. Next evening the QRS conduction time had fallen to 0 08 sec., and bundle branch block was no longer present, but right axis deviation persisted. The patient still showed signs of pulmonary edema. Diuresis occurred and the patient began to improve. Changes toward normal in the electrolyte pattern (Fig. 65) occurred later. The calcium levels were not increased. The right axis deviation became less marked over the following two weeks but was still present on discharge from the hospital.

There is a question whether the electrocardiographic abnormalities in this patient were not due in part to the low sodium and in part to the high potassium The potassium levels were increased and were in the zone wherein electrocardiographic changes were recorded by Tarail. From the extent of the QRS abnormalities we had expected that a higher potassium level would be found. It is recalled that in this case the normal activity of the sinus node was preserved, while in the cases reported by Stewart, Shepard, and Horger auricular standstill was found at the level of 10 mEq/L. It is possible that the level of potassium in the serum did not reflect the concentration of potassium in the cells, or that the low sodium made it possible to have these electrocardiographic abnormalities at a lower level of serum potassium.

Hypopotassemia

Electrocardiographic Signs

Recent observations of Bellet and his associates on the association of electrocardiographic changes and hypopotassemia may be summarized as follows. They recognized five electrocardiographic patterns due to low potassium: (1) depression of RS-T segments of varying degree, most commonly associated with vomiting; (2) inversion of the T waves, found most commonly in diabetic acidosis; (3) T waves of normal amplitude with prolongation of the Q-T interval; (4) low amplitude of the T waves; and (5) prominent U waves. These electrocardiographic abnormalities due to low potassium were immediately reversed following the administration of potassium. Bellet, *et al.* were of the opinion that the appearance of the U wave and lengthening of the Q-T and of the Q-U intervals are important criteria of low potassium. In some instances of alkalosis diminished serum or ionizable calcium probably contribute to the electrocardiographic changes. When

blood sugar 92 mg, carbon dioxide 53 volume per 100 cc, chlorides 98 mEq, serum protein 5 Gm, sodium 132 mEq, potassium 2.2 mEq., and calcium 6.3 mg. per 100 cc. The electrocardiogram showed prolongation of Q-T time. It was finally recognized that the patient's symptoms of weakness, prostration, and fainting were due to hypopotassemia. For months she had been losing potassium by diarrhea through the colostomy drainage as well as in the vomitus. None of this loss had been replaced in the infusions which had been given. In the short intervals during which the patient ate sparingly this ion was not adequately replaced. She

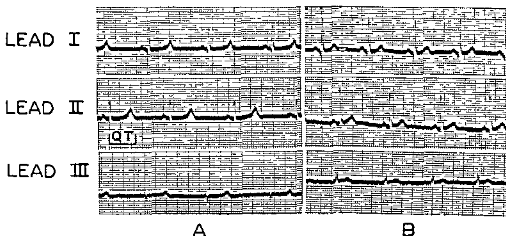


Fig 67

Electrocardiographic Changes in a Woman 21 Years of Age who Suffered from Hypocalcemia due to Hypoparathyroidism following Injury to Parathyroid Glands during Thyroidectomy.

51 of Q T time to 0 48 second, heart rate being on the average, upper limit being 0 46 second id 7 mg per 100 cc, that is to say it was low, normal level being 9 to 11 mg per 100 cc Thyroid extract, AT 10, and calcium lactate were being given

B was taken December 28, 1944 Q-T time was 0 36 second Heart rate was faster, being 60 per minute Serum calcium at this time was 12 mg per 100 cc

Patient was on a regimen of vitamin D, calcium lactate, and thyroid extract

was given modified Darrow's solution in glucose by hypodermoclysis. This solution contained sodium chloride and potassium chloride, 2 9 and 2 7 Gm per liter respectively, whereas Darrow's solution contains 4 0 Gm and 2 7 Gm respectively. There was immediate dramatic improvement with disappearance of weakness and prostration, and reappearance of normal strength Electrolytes were maintained by intravenous infusions, calcium being added There was a gradual return of serum potassium to normal levels. Three days after institution of this therapy the blood urea nitrogen was 11 mg per 100 cc, sugar 84 mg, carbon dioxide 65 volume per 100 cc., chlorides 95 mEq, serum protein 5.4 Gm, A/G ratio 3.3/2.1, serum

there is combined hypocalcemia and hypopotassemia, the administration of both calcium and potassium is necessary to restore the electrocardiogram to normal configuration.

Tarail has described low amplitude of T waves and prolongation of electrical systole in patients with renal insufficiency with hypopotassemia.

The symptoms of weakness and the electrocardiographic abnormalities are promptly dissipated by the administration of potassium salts.

Periodic Familial Paralysis

Periodic familial paralysis is a congenital disease, characterized by transient paralysis and episodes of muscular weakness which are relieved by the administration of potassium salts. During crisis in this disease the striated muscles become flaccid and the respirations are gasping due to paralysis of the diaphragm and intercostal muscles. The cardiovascular manifestations consist of increase in pulse pressure, low diastolic blood pressure, collapsing pulse, increase in cardiac dullness, systolic murmur, high venous pressure, and marked electrocardiographic changes. All these changes are reversed by the administration of potassium.

ELECTROCARDIOGRAPHIC CHANGES. Stewart, Smith and Milhorat have reported a case demonstrating the cardiac changes occurring during paralysis and after recovery. During paralysis, when the serum potassium was low, there was slurring of the S waves with widening of the QRS complexes, the QRS running on up into the T waves which were decreased in amplitude and rounded and flattened (Fig. 66). After the administration of potassium chloride, which resulted in recovery from paralysis, the serum potassium increased and the electrocardiogram reverted to its usual configuration.

Because of the interrelation of glucose and potassium metabolism, Gass, Cherkasky, and Savitsky have succeeded in inducing attacks of familial paralysis in susceptible patients by either parenteral injection or ingestion of glucose. Typical electrocardiographic changes were recorded They were able then to alleviate all of these manifestations by the administration of potassium chloride.

Case Illustrating the Correlation of Clinical and Electrocardiographic Manifestations of Potassium Loss

I have recently seen a patient suffering from chronic ulcerative colitis and regional ileitis in whom colectomy and ileostomy had been performed She experienced prolonged attacks of vomiting and was losing approximately 1000 cc. of fluid daily from the ileostomy. A Miller-Abbott tube was in place for long periods of time. For many days she had been given no fluids by mouth but had received 10 per cent glucose and water intravenously. She complained of great weakness, and fainted. At this time the blood urea nitrogen was 74 per 100 cc, the chlorides (as sodium chloride) were 55 mEq., and the serum protein was 7.4 Gm. per 100 cc. Two weeks earlier the blood urea nitrogen and chlorides had been 22 mg. and 87 mEq/L. respectively. A transfusion was given, as well as salt solution by infusion One week later the patient fainted again and complained of weakness. Four days later there was extreme prostration (the patient could barely move) and the blood pressure was 80/52 mm Hg. The blood urea nitrogen was 10 mg. per 100 cc,

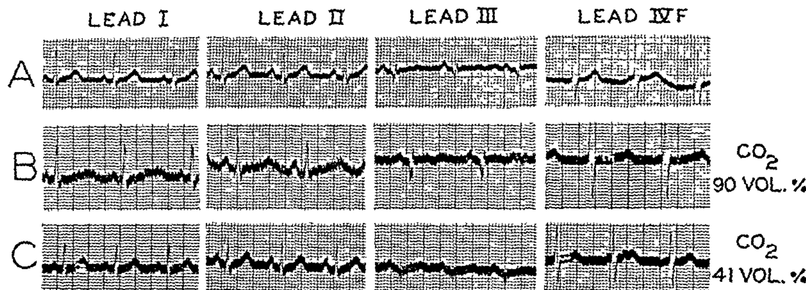


Fig 68

Electrocardiographic Changes in a Woman 69 Years of Age who Developed Alkalosis and Showed Marked Prolongation of Q T Interval Following Prolonged Use of One sixth Molar Sodium Lactate Intravenously

This patient had a carcinoma of ascending colon which was resected With Murphy button anastomosis was established between end of terminal ileum and side of transverse colon on July 9, 1946 Patient was on Wagensteen drainage and received 1000 cc one sixth molar sodium lactate intravenously daily for five days and sulfadiazine She became disoriented and lethargic and had a clonic convulsion on July 16

A, the control electrocardiogram taken July 3, was essentially normal

B, taken July 16, when patient was disoriented, showed marked prolongation of the Q T time to 0 64 second, the normal being 0 27 and the upper limit 0 394 second CO_2 combining power at this time was more than 90 volumes per 100 cc, serum chlorides 349 mg per 100 cc (60 mEq/L). At this time lactate and Wagensteen drainage were discontinued and patient improved immediately

C, taken July 21, shows restoration of electrocardiogram to its control configuration CO_2 combining power was 41 volumes per 100 cc Q-T time was 0 32 second, normal being 0 341 for this rate

potassium 5.1 mEq., and serum sodium 132 mEq. Four days later the electrocardiogram showed slight regression toward normal. At this time the serum calcium was 8.5 mg. per 100 cc Three days later still—ten days after starting the potassium replacement—the serum potassium was 6.0 mEq (slightly elevated) and the serum sodium 122 mEq This case is cited to illustrate the importance of maintaining a balance of ions.

It might be well therefore to keep in mind weakness as a manifestation of hypopotassemia and to make provision for the restoration of potassium given orally or by using *modified* Darrow's solution We have become accustomed to using normal salt solution for many purposes, but should also bear in mind that maintenance and restoration of other electrolytes may be necessary.

Prolongation of Q-T Interval

The Q-T interval in the electrocardiogram may be prolonged in *hypocalcemia* (Fig. 67). The level at which these changes occur has not been accurately established The Q-T interval may be prolonged in hypocalcemia occurring in hypoparathyroidism resulting either from a tumor, from complete surgical removal of the parathyroid glands during parathyroidectomy, or from their removal inadvertently during thyroidectomy. Hypocalcemia is seen in renal insufficiency with uremia; it is seen in alkalosis, it may follow profound diuresis with the loss of calcium; it occurs after prolonged diarrhea such as takes place in colitis or sprue; and it is recorded in excessive vomiting It is not uncommon in our clinic, where frequent serial electrocardiograms are taken, for manifestations of this chemical disturbance to be recognized electrocardiographically before it is suspected clinically. The differentiation of prolongation of the Q-T interval due solely to low calcium and that due solely to low potassium has been described on page 516

Calcium gluconate given intravenously may be effective in alleviating the symptoms of hypocalcemia found in *hypoparathyroidism* Uremia is treated in the usual manner. The electrocardiographic pattern of acute uremic pericarditis—which in uremia may occur without pain—may be superimposed upon those relating to the changes in blood chemistry The primary cause of diarrhea is treated when this is the cause of the chemical defect Govan and Darrow have devised a solution comprised of sodium chloride, sodium bicarbonate, and potassium chloride for parenteral use in infantile diarrhea, which has resulted in a substantial decrease in mortality

The cause of the prolonged Q-T interval in patients with recent *myocardial infarction*, especially those with posterior base pattern, is not apparent. Prolongation of the Q-T time in *diabetic acidosis* has been related by Nadler, Bellet, and Lanning to depression of the serum potassium The interrelation of ions is such that the resultant electrocardiographic pattern reflects the composite electrolyte pattern and it may not be possible at the present time to separate specific effects

Shortening of Q-T Interval

In hyperparathyroidism the Q-T time is shortened and prolongation of P-R time may occur in association with increase in the concentration of calcium in the blood. Both these abnormalities are alleviated on surgical removal of the abnormal parathyroid tissue.

Occasionally the changes in the several components of the electrocardiogram may be indicators of electrolyte changes in the blood. It must be kept in mind that changes in concentrations of the serum electrolytes need not reflect the actual concentration within the cells. The electrocardiographic pattern is frequently a reflection of the summation of different electrolyte effects. Moreover, the electrocardiographic pattern cannot be interpreted in terms of functional capacity. It can be inferred nevertheless that the integrity of the circulation cannot long be maintained in the presence of certain cardiac rhythms which result from electrolyte alterations.

Care should be exercised, in the treatment of the patients exhibiting the aberrations which have been briefly described, to bring about restoration and maintenance of electrolyte balance as well as of fluid balance This phase of medicine is only beginning to receive attention. Its further exploration may be expected to yield far-reaching therapeutic benefits.

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Effects of Alkalosis

The cardiovascular disturbances which may occur in alkalosis are described in Chapters 27 (p 480) and 30 (p. 507). Alkalosis with rise in carbon dioxide component of the blood together with mental changes may result (1) from the use of one-sixth molar sodium lactate intravenously to prevent crystalluria when sulfonamide drugs are given; (2) *when bicarbonate of soda is given by mouth for the same* purpose; (3) when prolonged aspiration of the stomach contents occurs with the loss of chloride, (4) from the prolonged use of alkaline powders in the treatment of gastric ulcer; and (5) rarely, if excessive diuresis is undertaken by daily mercurial diuretics.

Electrocardiographic Changes

The electrocardiographic changes in these states are characterized by flattening and undulations of the T waves and prolongation of the Q-T interval (Fig. 68). These alterations may be the early signs pointing to disturbances in electrolyte balance before *they are suspected clinically. Especially is this the case unless* chemical analyses of the blood are done frequently.

Treatment

The first measure in the correction of this aberration in blood chemistry is to discontinue the offending drugs or procedures, this alone may be sufficient to allow recovery. On the other hand more strenuous measures may be indicated, such as the use of ammonium chloride by mouth or parenterally In the latter case, 20 Gm. is given intravenously as a 2 per cent solution over a period of approximately three hours.

SUMMARY

The effects of certain disturbances in electrolyte balance on the cardiovascular system have been briefly discussed. These changes may be brought about by primary increases or decreases in essential electrolyte components of the cells and of the fluids bathing these cells These alterations may be in turn due to changes in the electrolyte composition of the blood. Disturbances in the usual electrolyte pattern may be brought about in a variety of ways. Electrolytes may be lost from the body in the vomitus, by diarrhea, by suction of fluids from the gastrointestinal tract by Miller-Abbott or Wagensteen tubes, by excessive excretion of certain ions, and finally as a characteristic feature of a disease. In other instances the concentration of certain electrolytes in the blood serum is increased. The increased concentration may be related to several factors, namely increased ingestion of certain electrolytes, decreased excretion of them, breakdown of cells, and finally the underlying characteristics of a disease.

In both instances, namely a decrease and an increase in concentrations, certain *functional disturbances* result in various organs of the body when the concentrations reach a certain degree below or above normal. The effects of some of these alterations on the cardiovascular system have been briefly described.

CHAPTER 32

What to Tell Patients About Their Heart Disease

Patients make many inquiries when they are told that they have some form of heart disease A majority of these can be anticipated by the physician and answers prepared for them beforehand

Patients want to know how long they will be sick, how long they will be incapacitated, how long they will have to remain in the hospital or at home in bed, and how long a convalescence is indicated before they can return to work. Many of these questions cannot be answered at once but will have to be met as the course of the patient's disease unfolds. I have indicated in the treatment of most of the cardiac conditions how each of these inquiries should be met. It is much the better course not to make any definite promises about these periods in order to avoid disappointment if a change in plans should be found necessary.

EARLY ADVICE

In most instances adult patients should be given a definite diagnosis of their disease as soon as possible This should be interpreted in terms of necessary medical care in the immediate future Depending upon the disease and upon how sick the patient is, some immediate orientation may be required concerning the future after the next few weeks or months. Acutely ill patients should be reassured about their present state, leaving for discussion during convalescence the effect of the disease on the patient's future health and business This allows the physician an opportunity to appraise the effect of the disease and helps the patient to attain some measure of adjustment to his illness. It is not possible to secure complete cooperation of the patient unless he has an understanding of the reasons for the treatment measures, for rest in bed, and for the entire regimen. It is better, for

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The executive with a cardiac disorder may be able to continue most of his activities. After coronary thrombosis, patients may get back to full essential activity after the superfluous elements have been discarded. Care should be exercised that lunch time is kept free of business; a rest after lunch at the office may be advisable. The patient's outside activities must be assessed and decisions made about golf and other games.

Many women can manage all or a part of the housework. This must be discussed with the patient. She should be made to see that it is better for her to remain well and at home even on limited activity than to attempt to do too much of the housework, and run the risk of a recurrence or an exacerbation of her illness. Assistance may be supplied by the husband, children, relatives, hired help, or help contributed by relief agencies in order to keep the household going. The household activities may be reoriented and the kitchen redesigned so that the work is accomplished with minimal effort.

The patient should be advised how to return to work after his illness. Cooperation of the employer may be enlisted Each case must be individualized. Exact advice is given; the way to carry on must not be left to the patient's discretion. It is frequently advisable to start working part time and then gradually work up to a full day's work even when there has been a prolonged and adequate convalescence This affords an opportunity to get back into the swing of working without a setback and without undue fatigue The patient's activities should not be set up too far ahead with the vague advice "not to do too much" A list of recommendations which make up the schedule should be compiled rather than to trust the patient's memory: the medications, when and how they are taken, the fluid intake, and instructions about diet When special diets are required it will be necessary to tell the patient or a member of the family how the food should be prepared, especially with respect to the use of salt

CHILDREN

Children may be accorded the same approach when they are old enough to understand simple descriptions of the illness and can cooperate in carrying out the regimen I think this approach is possible to follow in such a way that the child retains a healthy, normal outlook "Heart consciousness" need not be induced.

For the cardiac child who is attending school, the difficulty in getting to school, the number of stairs to climb, and the availability of elevators should be investigated. Activities should be based upon the patient's functional capacity. The physician should decide about climbing stairs, whether gymnasium is permitted and in what form, what games may be played, the possibility of baseball, swimming, or bicycling, and what kind and amount of after-school play are advised. The patient should be made to see that childhood and play cover a short space in the over-all life span, that these are brief periods leading toward adult life, and that childhood games and activities will take on less importance within a few years. As the child grows older and new interests appear, his activities should be re-evaluated at least once or twice a year During these early years, the patient's interests with respect to his life work or trade might be turned toward something compatible with his

instance, to inform the patient with myocardial infarction about what has occurred and what the immediate plan is, than to temporize from day to day and to have the illness stretch out and keep the patient in the dark about what is in store. The sooner the patient adapts his mental attitude to the regimen and its restrictions, the greater will be the benefit derived from the relaxation. Each illness requires a different approach. The patient should be apprised of his disease in simple words: its meaning in terms of the functional capacity of the heart, and the objectives of therapy.

The patient can be indoctrinated gradually in the physician's objective as convalescence proceeds. This part of therapy has been stressed in the treatment of each disease as it has been discussed. When an ambulatory patient is seen on several visits for an evaluation of his cardiac status and for therapy, if any is required, it is the best course to reassure the patient at the earliest visit and to save a discussion of the diagnosis and formulation of plans of therapy until all of the data are available. This avoids a piecemeal discussion without an over-all view. This, of course, is not the approach if the patient is in need of immediate therapy.

RETURN TO WORK

The patient wants to know when he can go back to work. It has already been pointed out that this subject must be discussed with each patient. The decision is based upon the patient's functional capacity, his therapeutic classification, and the kind of work the patient does. What each occupation involves, from the farmer to the industrial worker, must be analyzed. If it appears that the patient should not return to his former occupation, placement in a more suitable job should be attempted. This is one of the most important phases of the after-care of a patient. It is a great economic waste and the cause of unnecessary suffering for a patient to attain a certain degree of cardiac reserve after recovery from congestive heart failure, and then to be sent back to a job which is too strenuous, only to experience a recurrence of cardiac decompensation

OCCUPATION

Cardiac patients can find many occupations which are compatible with their functional capacity. The physician should try to adapt the patient to his present occupation, or the occupation to the patient. How the patient travels to work, the hours, whether climbing stairs is necessary, all have to be taken into account. Analysis of the work the patient is required to do should be made, to see that it is not beyond his functional capacity. Cardiac patients for the most part should avoid occupations which entail walking up and down many stairs and should avoid carrying heavy sample cases such as a salesman might need to do. Driving a truck is usually too strenuous. There are many jobs on light assembly lines in industry which require workers to sit down; these are especially suitable for cardiac patients No useful contribution would be made by compiling a list of occupations a cardiac patient can engage in. It is more important for the physician to consider each patient in connection with each individual job.

hold down their jobs and to have economic freedom rather than to expend too much energy trying to "keep fit" by exercise. The margin between cardiac compensation and heart failure may be small.

Patients should avoid sudden acute or prolonged efforts, such as lifting or carrying heavy objects, walking against the wind, or shoveling snow in the cold and wind

The rationale behind these limitations is based not only upon clinical experience but also upon functional tests. Hickam and Cargill have shown that patients with valvular heart disease who have suffered from congestive heart failure may have at rest the largest cardiac output that they can achieve. An oxygen debt is thus created by any attempt to meet additional demands which must later be repaid Exercise under these circumstances requires widening of the arteriovenous oxygen difference (Chapter 1).

SPAS

I have had little experience with spas and health resorts in the treatment of cardiac patients Patients with all the manifestations of cardiac diseases can be adequately cared for without their use The people in the United States have not become conditioned to this form of therapy as is the case in European countries It is likely that much of the benefit from spa therapy is derived from the regimen, the relaxation, the absence from business, and the restriction of food intake when this is a feature, rather than from the baths or waters Cardiac patients should not be subjected to the extremes of hot or cold baths because these make excessive demands on the heart to accommodate for the rapid changes in the vasomotor system. Hot baths may cause hyperpnea with alkalosis and loss of carbon dioxide On the other hand many patients who would not go away on holidays or lead sensible lives during them can be persuaded to take "cures."

SMOKING

The patient may inquire whether he may continue to smoke, or the physician may raise the issue. The question of smoking has been discussed in Chapters 12 and 13, and will be mentioned only briefly here. Smoking increases the heart rate, increases the blood pressure, may increase the cardiac output, decreases the peripheral blood flow presumably by vasoconstriction, and makes the fingers and toes cold (Stewart). Observations have shown that vasoconstrictor effects of nicotine on the cardiovascular system cannot be counterbalanced or prevented by the vasodilator effects of alcohol If a subject smokes frequently these effects may persist from one period of smoking to the next and be present continuously through a large part of the day. In susceptible persons there may be decrease in amplitude of the T waves of electrocardiograms Levy has shown that the injection of nicotine bitartrate intravenously in 2.0-mg amounts induces certain of these effects. Patients who have angina pectoris or who have suffered myocardial infarction, or who have peripheral vascular disease should not smoke Patients with congestive heart failure from any cause should stop smoking until compensation is restored. Whether smoking is permitted

functional capacity and economic status. Establishing a good rapport with a child and having the relationship grow and change dimensions with adolescence and adulthood are constant challenges to the physician. During adolescence there is a great urge to conform to what the other children do With the approach to the college age, there is not so much inclination to do the same things, so that more independence is possible without appearing to be out of step, and many of the problems of long-time management are more easily resolved

RECREATION, ATHLETICS, AND EXERCISE

Patients want to know the recreations, athletic activities, and sports they can engage in One of the most difficult patients to convince about the wisdom of the reduction of activities is the man who has continued to engage in athletic games because he has always done so, who has kept up the same strenuous sports although growing older, and who is unwilling to admit that he cannot do as much as he could do several decades earlier When these patients yield finally to advice they may admit that they have not enjoyed strenuous exertions for some time, that they were in fact made uncomfortable by them, and that they only kept up the exercise in order not to admit that they were getting older Other patients suspect that they are "growing soft" when they experience the onset of cardiac symptoms with dyspnea, and will embark on a renewed period of training and gymnasium work in order to "get back into form" From this misguided notion irreparable harm may result

When games are permitted in the regimen of cardiac patients they should be played for fun and exercise and not in competition.

Swimming is permitted to some cardiac patients provided they do not get into situations where they cannot rest at once should they experience fatigue, dyspnea, or pain They should not swim in rough or in cold water, chilling should be avoided Sitting around in wet or damp bathing suits is not advisable, especially for patients who have had rheumatic fever In certain patients bathing without swimming may be permitted

Sun bathing in moderation may be advised for certain patients but overexposure and toxic effects of the sun must be discouraged Patients with hypertension should avoid long periods of exposure to the hot sun

Tennis may be permitted for some patients with good functional capacities It is best, however, that playing be restricted to doubles in order to avoid the strenuous running which singles requires.

Golf may be an effective recreation The number of holes may be gauged to what the patient can do without dyspnea and undue fatigue Hilly and difficult courses should be avoided

Walking may provide a certain amount of recreation and exercise for patients whose functional capacities are limited. Patients who have suffered from congestive heart failure or in whom the cardiac reserve after recovery is restricted are made to see that they do enough walking and moving around in the course of a day's required activity to make any special effort at walking for exercise unnecessary. It is much more important for their economic status and for their mental attitude to be able to

is not used to take the place of food. In older people a small drink of whisky at bedtime may serve as a good sedative.

Patients who have had myocardial infarction or who suffer from angina pectoris should exercise care that they do not overeat or overdrink at mealtime. A glass of *wine with meals* may be permitted to some patients, but it should not be used to the extent that too great a sense of well being results so that more food is eaten than is wise. A vicious cycle may be started, with overdistention of the stomach. These are problems that have to be met in a great number of patients.

SEXUAL INTERCOURSE

Patients with chronic organic heart disease and those who have recovered from cardiac affections are likely to make inquiry about the effects of sexual intercourse, and will wish to know how soon such relations may be resumed. Even though the inquiry is not made, the physician should nevertheless advise the patient on this score. Many patients during illness experience a decrease in libido which is corrected with recovery. Pericardiectomy for chronic constrictive pericarditis may result in recovery of libido and sexual capacity. Patients should be reassured on this point. Most patients with organic heart disease with good functional capacities need not take special precautions about sexual intercourse. Advice is required, though, for patients suffering from angina pectoris, for patients after myocardial infarction, for patients with chronic congestive heart failure, and for those who have recovered from congestive heart failure.

A frank discussion is undertaken with the patient about the occurrence of symptoms during intercourse, how soon the symptoms disappear, the duration of the preliminary precoital play, and the duration of intercourse before orgasm occurs. It may be that with cooperation of the partner, adjustments can be made in the patient's usual pattern so that intercourse may be indulged in without too great cardiovascular strain. Boas has recorded certain effects on the cardiovascular system and on the heart rate during intercourse. Depending on the severity of the myocardial infarct, and the rapidity of convalescence and of restoration to normal activity, intercourse may be first indulged in two to three months after the attack. This period of abstinence is easier for patients in the hospital than for those treated in the home.

Patients who have severe angina during or after intercourse should abstain. The use of nitroglycerin beforehand might be tried in patients with great sexual drive who experience tension when intercourse is denied.

The advisability of allowing pregnancy to occur in cardiac patients is discussed in Chapter 28.

SLEEP

Patients with heart disease should plan their activities so that they have adequate rest. Those who are heads of families or have to earn a living may be required to go to bed early in order to maintain an adequate reserve. Other patients may find it beneficial to remain in bed part of the weekend. Those who do not go to

later depends on the amount of reserve which has been regained. It is obvious that patients who have any symptoms while smoking should not smoke.

There probably is no occasion for patients with asymptomatic rheumatic heart disease or with many of the other forms of heart disease to discontinue smoking if they have no distress from it. There are, however, some persons with apparently normal cardiovascular systems who are sensitive to tobacco. They experience palpitation, precordial distress, and cardiac irregularity, usually owing to ventricular premature contractions after smoking. Abnormalities of the T waves of the electrocardiograms may be recorded in susceptible individuals after smoking only one or two cigarettes.

Advice about smoking may be altered to suit the occasion for aged people whose life expectancy is short. The increment of longevity which might be attained would not compensate for the distress caused by changing a long-established habit.

ALCOHOLIC BEVERAGES

For certain patients the moderate use of alcohol may be considered medicinal and is recommended, provided there are no contraindications. In this category are patients suffering from hypertension, patients with coronary artery disease and angina pectoris, and patients who have sustained myocardial infarctions. If alcohol relaxes the patient or relieves the pain in angina pectoris, it serves a useful purpose. It should not be used if untoward symptoms such as palpitation or tachycardia result. I have not seen harm from its medicinal use, nor have I seen it serve as an escape mechanism in patients with organic heart disease, when its intelligent use was recommended I have seen patients who have used alcohol to excess, as an avenue of escape, come to have hypertension and various forms of organic heart disease, but the pattern for the abnormal use of alcohol was present beforehand

When alcohol is used as medicine the amount should be prescribed as well as the number of drinks a day and how the alcohol is to be taken. Patients who are on limited fluid intakes should not take highballs or "long drinks" as these count toward their total fluid intake for the day. I believe that plain water is better for most patients than charged water when diluents are used, the carbon dioxide in charged waters may lead to abdominal distention For this reason *champagne* may not agree with some cardiac patients. *Beer* is also not recommended because of the volume of fluid and the carbonation

Many patients who suffer from angina pectoris experience discomfort after taking a highball or a beverage which is very cold and contains a great deal of ice. Some patients have found that whisky diluted slightly with tap water at room temperature without ice resulted in a feeling of relaxation without any discomfort Incidentally this is a satisfactory and palatable form in which to prescribe medicinal alcohol. For the most part, simple alcoholic beverages are more satisfactory than complicated ones. Those containing syrups and sugar may make the patient more thirsty than their allotted fluid intake will allow them to satisfy

When alcohol is recommended to patients whose appetites are increased by it, the food intake should be watched to prevent an undesirable gain in weight. On the other hand, to avoid the risks of avitaminosis, care should be exercised that alcohol

for continuous or emergency use, should the cabin be pressurized. Many patients who have recovered satisfactorily from myocardial infarction with good cardiac reserve will have no discomfort. It is recalled that the Levy anoxemia *test for* the detection of coronary insufficiency depends on the breathing of a 10 per cent oxygen-90 per cent nitrogen mixture for a period of 20 minutes or until the onset of pain. Breathing this mixture is equivalent to flying at an altitude of approximately 18,000 feet. Flying at an altitude of 10,000 feet in an unpressurized cabin provides an atmosphere of approximately 14 per cent oxygen In most instances when pressurization is provided the cabin pressure is maintained to approximate the pressure at 8000 to 9000 feet. It must be kept in mind that if anything goes wrong with pressurization at a high altitude the consequences might be harmful or fatal to a cardiac patient, though the low oxygen pressure at this altitude is safely managed by a normal person

Acute heart failure has occurred during anoxemia tests and presumably may also do so in flying With suitable precautions and with careful selection of patients, however, this accident can be avoided Certain patients with marked coronary artery disease may breathe low concentrations of oxygen without experiencing pain.

Under most circumstances patients suffering from *congestive heart failure* or from the cyanotic forms of *congenital heart disease* should not travel by air. Circumstances might arise, however, which might make air travel necessary The flight might be accomplished in safety at a low altitude or by the continuous inhalation of oxygen Patients with *compensated rheumatic valvular lesions* usually fly without discomfort, the same precautions with respect to availability of oxygen and pressurization are maintained as for normal subjects I have seen patients with *auricular fibrillation* who were adequately digitalized and in a state of compensation travel comfortably by air without symptoms and feel better on arrival than when the same trip had been taken by train Patients with congenital complete *heart block* without other congenital cardiac anomalies and with good functional capacities might be permitted to travel by air, while the patient with acquired complete heart block—usually resulting from arteriosclerotic heart disease—might be warned against flying.

Patients should be advised to *avoid gas-forming foods* before air travel. Carbonated beverages may augment abdominal distention with the increase in altitude which may give rise to discomfort and cardiac embarrassment Small meals should be eaten in transit Moving around in the plane should be restricted as much as possible Air travel is usually easier for those who have previously used this form of transportation First flights for cardiac patients may induce tension which might be harmful

Air travel for patients having *pulmonary disease* with cardiac *manifestations* requires careful deliberation. Patients exhibiting pulmonary fibrosis, pulmonary emphysema, asthma, and chest deformities need special consideration At sea level the pulmonary ventilation and the arterial oxygen saturation of such patients may already be greatly diminished Further reduction of the arterial oxygen *saturation* as well as further demands upon the pulmonary exchange should therefore be avoided Air travel should be forbidden if moderate exertion causes excessive dyspnea Oxygen should be available if flying is permitted.

Patients with marked *anemia* should not travel by plane because the decrease *in*

business may find it expedient to rest a part of the day in the middle of the week Adequate sleep is recommended to all, but it is essential for the cardiac child and for persons who have recovered from rheumatic infection. This precaution may go a long way toward providing for resistance to respiratory infections. One late night a week may be permitted when the sleep which is lost can be made up the following morning Many patients acquire the habit of resting after lunch or before dinner, a regimen that can perhaps be continued to advantage throughout life Many business executives can manage after lunch to rest lying down and without appointments for one-half hour to an hour Convalescence from an illness affords an excellent opportunity to acquire habits of sleep and rest which can be adhered to after recovery. While patients are sick, mild sedatives such as phenobarbital or pentobarbital may be required to provide sleep. With recovery and activity they are no longer necessary, but the dosage may be cut back slowly in order to avoid withdrawal symptoms. Many business or professional people who have to face difficult situations the next day find it difficult to sleep the night before, and when they finally resort to medication there is not time for the effect of the drug to be dissipated before the patient must get up When it appears necessary, it seems to me much better for the patient to take the medication early, enjoy a good night's sleep, and be ready for the activity of the day. The medication should be taken without a conflict and sense of inadequacy or guilt

HOBBIES

Cardiac patients may find it expedient to cultivate hobbies. These avocations should not be transient fancies. They can be so chosen that growth and breadth of interest increase with age The choice should be commensurate with the patient's present and expected functional capacity Hobbies can frequently be turned to gainful ends.

AIR TRAVEL

With increase in air travel the physician is more and more called upon to decide about the advisability of this form of travel for cardiac patients There have been few cardiac accidents in the total number of patients who have traveled by airplane The recommendation is based on the distance, the altitude at which the plane is expected to fly, the availability of oxygen, and whether the cabin is pressurized. The patient's functional capacity and the difficulties of alternative forms of travel are taken into consideration For example, it may be more expedient for the patient to take a short plane trip at a low altitude than to have to go to the railroad station, walk long distances, and be uncomfortable many hours on the train. A patient who has suffered a myocardial infarction and has made a satisfactory recovery may be moved by plane at a low altitude on a clear day or in a pressurized plane with much less effort for the patient and with less encroachment upon cardiac reserve than by motor or by train

Patients who have angina pectoris as well as those who have had recent myocardial infarction should not travel by air unless oxygen can be made available

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patient to travel by air. If a satisfactory functional capacity has t might be sanctioned if the circumstances warranted it.

ve acute respiratory infections, especially those with rheumatic ld not travel by air. If it should be necessary, the use of vaso- such as neosynephrine and benzedrine sulfate before and after keep the eustachian tubes patent Patients with chronic sinus se vasoconstrictor drugs in the same fashion. Unless it is abso- tients with acute sinusitis should not travel by air.

AIR SICKNESS

ve air sickness may be given phenobarbital in the usual doses ine hydrobromide, 0 0006 Gm. by mouth one hour before flight e time of flight, may be effective in preventing motion sickness ercial preparation which has been found to be effective. Drama- ntihistaminic drugs, has been successful in controlling all forms s—air, car, and sea. Gay and Carliner recommend that 100 mg. tes before the flight begins This amount may be repeated every s necessary The patient should be warned of the possibility of

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preceded by attacks of acute upper respiratory infections, acute tonsillitis, or "common colds," but the factors which determine when attacks will be followed by rheumatic fever are not known Because of these associations all upper respiratory infections and attacks of acute tonsillitis should be given adequate treatment, especially in those subjects who are known to have suffered previous attacks of rheumatic fever. Respiratory infections in other members of the family are important as sources of infections for patients who have had rheumatic fever. It has been shown that recurrences of rheumatic fever can be prevented by the use of ration doses of sulfadiazine Ration doses of penicillin orally may prevent recurrences of rheumatic infection in children who have previously had rheumatic fever. Another approach is the early use of penicillin in all streptococcal infections. When patients suffer attacks of rheumatic fever bed rest should be provided over an adequate period of time in the hope that cardiac damage may not occur, or so that its effects may be minimized, and in order that the cardiac function may not be jeopardized by physical activity. The early use of ACTH may abruptly terminate an attack of rheumatic fever and prevent cardiac damage. However, this drug has been used too recently in the treatment of rheumatic fever for its role to be adequately assessed at the present time The patient's life after a rheumatic infection should be oriented in such a way as to prevent further attacks, forestall cardiac damage, avoid overstrain of the rheumatic heart, and regulate the patient's ambitions and efforts to gain a livelihood.

For a few susceptible persons residence might be changed to a tropical climate if this is feasible For younger patients, transient residence in a tropical climate until after adolescence may be of benefit The incidence of active rheumatic infection and of rheumatic heart disease is lower in the southern states than in the northern states. There is, however, too much communication between the two regions with the opportunity of transmitting respiratory infections for maximal benefit to be accorded susceptible individuals merely by going to the southern part of the United States

For patients with prolonged attacks of rheumatic fever and with active rheumatic carditis, prolonged residence in sanatoria or in convalescent homes for the special care of rheumatic fever patients may prevent recurrences and minimize cardiac damage or may prevent overstraining a heart which has been recently affected.

SYPHILITIC HEART DISEASE

This form of heart disease can be prevented The etiologic agent and the method of dissemination are known If syphilis can be eradicated syphilitic heart disease will disappear This is a public health problem of major proportions. By the maintenance of adequate prophylaxis during intercourse the incidence of primary syphilis can be sharply reduced. Moreover the prompt and adequate treatment of the primary disease can be expected to prevent almost completely the later development of cardiovascular syphilis.

CHAPTER 33

Prevention of Heart Diseases

What can be done in a positive way to prevent diseases of the heart? Something has already been said about the management of patients suffering from diseases which predispose to cardiac damage This chapter aims to recapitulate such information.

CONGENITAL HEART DISEASE

Since the cause of congenital malformations of the heart is not known, specific preventive measures are not possible Recently, however, it has been suggested that rubella during pregnancy predisposes to congenital malformations in the fetus The best that can be done at present is to provide good prenatal care in order to insure as normal a period of gestation as possible.

RHEUMATIC HEART DISEASE

Since the cause of rheumatic fever is not known, specific measures toward its prevention are not possible There are certain conditions, however, which it is believed predispose to the disease and which are susceptible to modification, correction, or treatment. It is known that the disease is most common among the children of the poor, under conditions of poor nutrition, inadequate clothing, unsanitary housing, and overcrowding It is most common in children of school age. Recurrences are more frequent in fall, winter, and early spring. Epidemics of rheumatic fever have occurred in households and in camps. There are reports of recurrences yearly in certain locations and certain houses. Some families are especially susceptible to this disease. It is most common in the north temperate zone, and rare in the tropics. There is evidence that beta hemolytic (Group A) streptococci are implicated. It is known that attacks of acute rheumatic fever are frequently

CORONARY ARTERY DISEASE, MYOCARDIAL INFARCTION

Since arteriosclerosis of the coronary arteries is the common forerunner of these conditions, special attention should be given to patients who have evidence of degenerative changes, especially of the coronary vessels. Even in the presence of good functional capacity of the heart, proper evaluation of T wave and RS-T segmental changes may deter or prevent more serious complications later. Patients should be told to live in a manner commensurate with their chronologic age or with the indicated age of the coronary vessels. Adequate rest, avoidance of obesity and excesses in diet, and regular vacation periods may be of benefit. Relinquishment of certain business activities may be indicated. For patients who already have symptoms of coronary insufficiency—for instance, angina—adequate appreciation of the symptoms and reorientation of activities and use of the medical agents described in Chapter 12 may relieve them of distress or make them more comfortable. By these measures coronary thrombosis may be delayed or, once it has occurred, further damage may be prevented Complete bed rest, anticoagulants and other drugs as indicated, and gradual restoration of activities following convalescence from myocardial infarction constitute the accepted forms of therapy (Chapter 13) There is not enough evidence available at the present time to warrant placing all patients suffering from angina or all who have recovered from coronary thrombosis on ration doses of dicumarol

THYROID HEART DISEASE

The serious cardiac complications of hyperthyroidism can be prevented by early recognition and treatment of this condition Especially is this important in the older age group, in whom coronary artery disease is an additional handicap

The early recognition of *myxedema* and its correction by the use of thyroid extract may prevent the progress of arteriosclerosis, and of coronary artery damage and thrombosis in these patients

ACUTE INFECTIONS

Prophylactic immunization against diphtheria has reduced the incidence of this disease and consequently of acute myocarditis with circulatory failure, formerly a frequent complication The early use of antitoxin when diphtheria is recognized reduces the likelihood of cardiac damage

The early treatment of acute infections with the proper antibiotics or other agents reduces the incidence of acute myocardial damage in these diseases.

Patients should be observed following acute *pericarditis* in order to detect the onset of chronic constrictive pericarditis This latter complication is not known to follow rheumatic pericarditis

ESSENTIAL HYPERTENSION AND HYPERTENSIVE HEART DISEASE

The cause of essential hypertension is not known. Since it is the forerunner of serious cardiac complications, its prevention would eradicate heart disease from a large segment of the population. Frequently this affection is familial. Moreover it is not uncommon for subjects who later become hypertensive to exhibit lability and transient elevations of blood pressure as well as transient tachycardia. Such persons should early be given advice about the cultivation of a serene attitude, the selection of work which is without tensions, and the avoidance of smoking and of all excesses. The program should include adequate rest, relaxation, and vacations; this program can be accomplished without making subjects over-conscious of their blood pressure. Routine follow-ups should be made at intervals in order to detect any changes which might indicate a change in regimen. Avoidance of obesity should be given strict attention. After the pattern of the hypertension has been established supervision should be maintained in an attempt to prevent cardiac damage and other sequelae. Consideration should be given to the advisability of thoracolumbar sympathectomy.

ARTERIOSCLEROSIS

The precipitating factors which lead to clinical arteriosclerosis are not known. This being the case, we have no reliable means at hand at present for the prevention of this degenerative disease or for altering its course. Recently the relation of cholesterol to arteriosclerosis has been assumed to be such a direct one that the use of cholesterol-poor diets has been advocated; for instance, the elimination of high-cholesterol foods and animal and vegetable fat from the diet has been recommended. We know too little at present about arteriosclerosis to try to prevent it in certain persons by drastic and prolonged alterations in dietary regimens. Subjects in whom the serum cholesterol and lipoproteins are high on repeated examinations should be given low cholesterol diets, a prolonged dietary regimen should not be set up on the basis of a single sample of blood, since the serum cholesterol is known to vary. Restrictions in the range of the Kempner "rice diet" may be required to bring about a fall in the level of the serum cholesterol. Recently, also, the ingestion of daily rations of choline and other lipotrophic agents has been advocated for the prevention of arteriosclerosis, but there is yet inadequate background for this form of therapy to have patients take these drugs over long periods. The natural history of arteriosclerotic processes is so variable in different individuals that nothing constructive can be gained by giving these drugs to a few patients. Undue gain in weight should be discouraged. Obese patients should reduce, and their intake of animal and vegetable fat should be restricted. Proper treatment of diabetic, nephritic, and hypertensive patients may prevent or delay the arteriosclerotic changes which are associated with these diseases. Barr recommends for all adult patients the avoidance of "surfeit, gluttony and obesity."

In persons of advanced age the history should take on a new approach. It is particularly important to uncover any symptoms which the patient has or any change in sense of well being so that study can also be turned in these directions. In this age group two-meter roentgenograms of the heart, electrocardiograms, and blood pressures are especially in order It does not appear feasible or wise to put all patients without symptoms through a routine gastrointestinal x-ray series unless there are symptoms which indicate that such tests are needed. The indiscriminate use of such investigations would not detect enough to make it worth the expense and the overburdening of x-ray departments If signs suggestive of disorder of any system appear appropriate investigations are made In many instances blood counts with differential and hemoglobin, routine urine, blood urea nitrogen, blood sugar, cholesterol, and uric acid may be required

After the survey is made the physician then has to decide what to tell the patient. The patient should not be burdened with details and descriptions about which nothing can be done Minor changes in the electrocardiogram should not be called to his attention. It is not my practice to give patients written reports of these examinations to carry around with them to be read over and over again Reports should be sent to other physicians as indicated Only when patients plan to travel and it appears wise for them to have essential data relating to their diseases with them is it my practice to give them summaries of their examinations to be presented to new physicians should they have occasion to require medical help when away from home

The physician who makes a health survey of a patient as a prophylactic measure assumes as much responsibility as when the patient comes to him suffering from certain complaints and having manifestations of disease. The patient should not be given a false sense of security by a perfunctory examination

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"ATHLETIC HEART"

It is now fairly well agreed that there is no such entity as an athletic heart. It was formerly thought that the hearts of athletes were large or showed hypertrophy. A normal heart can in all probability take care of the stresses and strains which are placed upon it by the rigors of participation in athletic sports, without any evidences of functional incapacity and without enlargement. It may be that those hearts which have shown enlargement after prolonged participation in games and sports were not normal beforehand and already exhibited congenital or rheumatic defects There is such variation in the size of normal hearts in relation to the body build that it would be difficult to be certain about small deviations from normal By the time athletes have come to the end of their life span and the hearts are examined it is too late to correlate the changes with athletic activity per se. If the hearts of a large enough number of young athletes who had accidental deaths were examined an answer to this problem might be available

Some precautions can be taken to prevent cardiac damage by participation in athletics Careful physical examinations should be made to insure that the hearts are normal beforehand. The response of the heart to exercise should be within the accepted experience for normal individuals During training athletes should be certain to secure adequate sleep, have proper food, and abstain from use of alcohol and from smoking

ROUTINE OR PERIODIC PHYSICAL EXAMINATIONS

The practice of routine or periodic physical examinations is a good one. It is not uncommon for babies to be examined at frequent intervals, especially during the various immunizations which are now routinely carried out Other examinations are made on starting school and entering high school as a part of the school health program. Again routine examinations are carried out on entrance to preparatory schools and college Many businesses have a program for physical examinations before engaging employees. Generally, however, health examinations have stopped at this point It is coming more to be the practice to have executives undergo periodic examinations and to have re-examinations of the employees at stated intervals, in addition to the follow-ups on those showing defects. Complete examinations at stated intervals are especially important in middle age

These routine or periodic examinations should not be perfunctorily and sketchily made. The objective is lost unless a sincere attempt is made to find out if the patient has any defects requiring correction or advice. A history which records the salient points should be taken. The heart and lungs in younger individuals are causes of chief concern. Murmurs at rest or after exercise should be adequately appraised. All available tests should be made to clarify this, including roentgenograms of the chest and electrocardiograms. It is now agreed that a roentgenogram of the chest is more satisfactory in the detection of minimal tuberculous lesions than is the physical examination.

intake and the diet at that time. Moreover, instruction should be given the patient or a member of the family about the preparation of the diet before discharge from the hospital. Ambulatory patients may require more time in orientation as they may not have had the benefit of orientation which hospitalized patients will have acquired. Specific instructions should be issued. Time can be saved by providing them with mimeographed forms or diet lists which are flexible enough to adapt to their needs. Instruction about the preparation of salt-free food requires individual attention.

PRINCIPLES OF DIET CALCULATION

Calculation of diet is not difficult if one keeps in mind the basic principle that all special diets are merely modifications of the normal one. Considering the normal diet to be basic, adjustments are made to suit the medical problem which exists, and, as far as possible, the food habits, tastes, and income level of the patient.

In determining the normal diet we must first know the energy requirement. This implies an estimation of the number of calories needed by the patient for basal metabolic requirements *plus* the calories demanded for his specific amount of activity. Tables VII and XI (p. 575) may be used for estimation of the energy requirement for patients if the average weight and grade of activity are known.

Table VII. Energy Requirements for Normal Diets
(Daily calories per kilogram of average weight)

Adults Degree of Activity						
Basal	Minimal (Bed rest)	Very Light (Typist)	Light (Student)	Moderate (Housework)	Heavy (Farmer)	Very Heavy
25	27.5	30-35	35-40	40-45	50-70	75

Children Age in Years								
Under 1	1-3	4-6	7-9	10-12	13-15		16-20	
					Girls	Boys	Girls	Boys
110	100-95	95-80	80-70	75-60	50-45	60-55	45-35	55-50

Having estimated the energy requirement in terms of calories per day, the next step is the division of these calories into the amounts of food constituents per day for optimal health. Protein, fats, carbohydrates, minerals, and vitamins must be considered. Protein, fats, and carbohydrates yield approximately 4, 9, and 4 calories per gram respectively. In the diet for adults, the protein should be included to provide 1.0 to 1.5 Gm. per kilogram of average body weight. In providing for the remaining calories, the fats and carbohydrates should be provided in a ratio of 35 per cent fat to 65 per cent carbohydrates. An example of this calculation follows:

A man whose average weight is 70 kilograms and who is engaged in office work would require daily 70 × 35 calories per kilogram of average body weight, or a total of 2450 calories. If the protein in his diet should provide 1.0 Gm. per kilogram,

CHAPTER 34

Diets in Heart Disease

The institution of proper diets and the management of fluid intake are important facets in the treatment of patients with heart diseases. In acute illness adjustment of the food intake to the condition of the patient and the stage of his disease is a critical need. In patients with myocardial infarction, for example, the diet may need to be changed in the early stages from meal to meal, and from day to day. Patients with congestive heart failure may require a succession of variations of salt restriction and diet with changes in their condition and with restoration of compensation and elimination of the excess body fluid Close supervision is essential to assess the effectiveness of the dietary regimen. It is well to see patients at mealtime to discover whether the orders are being carried out correctly, whether the food looks appetizing, and whether the patient is eating it With the onset of persistent nausea and vomiting or diarrhea care should be exercised that starvation acidosis does not ensue This may be detected by the presence of acetone on the breath or the appearance of acetone in the urine and by the high specific gravity of the urine. Fluids by hypodermoclysis, by the intravenous route, or occasionally by rectum may be required.

Care must be exercised that patients on restricted fluid intakes who are being given many medications do not use up their quota of fluids at odd times during the day in taking medicine. When it is possible, the medications may be given with the mealtime fluids or with the midmorning, midafternoon, or evening fluids.

It is recalled that many patients with chronic cardiac disease are in a state of poor nutrition and appear undernourished. This is especially the case in those with long-standing congestive heart failure and chronic constrictive pericarditis. This may be due to the long duration of passive congestion of the liver and of the gastrointestinal tract. It may not be advisable for these patients to gain much weight but provision for a balanced diet, perhaps with vitamin supplements, and improvement in the state of compensation result in a better state of nutrition.

When patients are in the hospital on special diets which must be continued after discharge, they should learn something about the management of the fluid

satisfactorily. It groups the vegetables and fruits according to percentage composition of carbohydrates. If it is impossible to include the protective foods in filling the diet prescriptions, mineral or vitamin supplementation should be ordered to make up the deficiency.

MEASURED FLUIDS

Very often in coordination with diet restrictions, particularly the low salt diets, measurement of the daily fluid intake is indicated. This includes milk, water, fruit juices, soup, soft drinks, coffee, and tea. Restriction of fluids to 1200 cc. in 24 hours permits approximately six ordinary table glasses (6- to 7-oz. tumblers). The best plan for dividing this amount is to allow one glass of fluid with each meal and another each in midmorning, in midafternoon, and at bedtime. This prescribed allotment of fluid should include the ordinary intake of milk and fruit juices or fluids allowed in accordance with any special diet which is ordered. Additional amounts may be made up with less important liquids such as water, coffee, tea, and soups. On a restricted fluid intake, when patients are not very sick, they prefer to use the required amount of fluids as water, fruit juice, and milk, rather than as soup. When the fluid allowed in 24 hours is 1500, 1800, or 2000 cc. it is divided proportionally and spaced evenly throughout the 18 waking hours.

It is apparent that it is circumventing the purpose of fluid restriction to allow 1200 cc. in 24 hours, for instance, only to have the patient supplement his diet with oranges, grapefruit, watermelon, canteloupes, plums, and other fruits of high water content.

LIQUID DIETS

On occasion a clear liquid diet is indicated, for temporary use only. It is difficult in this way to provide an adequate caloric intake. Such a diet cannot be made adequate for normal needs since it includes only the following:

Broth
Tea
Coffee (without milk or cream)
Ginger ale
Gelatin
Clear fruit juice
Sugar

A full liquid diet is employed when such a marked restriction is not required. This contains the following foods, all of which are liquid at body temperature:

Milk, milk beverages, and cream
Eggs (mixed into beverages)
Cereal gruels
Strained fruit and vegetable juices
Broth and strained cream soups
Vanilla ice cream, fruit ices
Jello without fruit or nuts
Sugar
Coffee
Tea
Carbonated beverages

70 Gm. would be required. Multiplying this by the factor 4, one finds that it would utilize 280 of the 2450 calories, leaving 2170 to be divided between fats and carbohydrates, thus.

$$\text{Fats} = 0.35 \times 2170 = \frac{759.5}{9} = 84.4 \text{ Gm.}$$

$$\text{Carbohydrates} = 0.65 \times 2170 = \frac{1410.5}{4} = 352.6 \text{ Gm.}$$

In round numbers the diet would therefore read protein 70 Gm (280 cal.); fat, 84 Gm (760 cal), carbohydrate, 353 Gm. (1410 cal.), making a total of 2450 calories.

For children, the same method is used but the optimal amounts of protein are increased to 2.0 to 4.0 Gm. per kilogram of body weight. The ratio of fat to carbohydrate is better at 30 per cent fat to 70 per cent carbohydrate

TRANSFERRING THE DIET ORDER INTO A FOOD PLAN

Once the amounts of protein, fats, and carbohydrates in the diet have been decided upon, the total amounts of food for the day, in terms of household measures, and its composition in terms of protein, fats, and carbohydrates* are computed to fulfill the diet prescription. In gauging the amounts of these foods allowed, one should keep in mind the protective foods of the adequate diet (Table VIII), the diet order, and the patient's food habits.

Table VIII. Protective Foods for Adequate Diet

Food	*Amount daily*
Milk	Adults—2 or 3 cups, Children—3 cups to 1 quart, Teen-age boys and girls, expectant or nursing mothers—1 quart
Egg	1 daily (or 4 to 5 a week)
Meat, fish, poultry	1 or more servings
Potato	1 or more servings
Fruit or vegetable	4 or more servings including citrus fruits daily and one green or yellow vegetable
Cereals and bread	Enriched and whole grain, 3 or more servings
Butter or fortified oleomargarine	1 or more tablespoons
Other foods to complete meals as desired and to fulfill individual energy requirements	

Food amounts should be stipulated as whole servings, for example glasses of milk, slices of bread, as far as possible. When the "foods for the day" have been listed, they should be divided into a daily meal plan to guide the patient concerning the foods he may eat, when he may eat them, and in what combinations. Some standard of describing the size of fruit and vegetable servings should be arranged; the one that accompanies the reducing diets in this chapter has been found to work

* These can be obtained from any satisfactory manual on food composition.

Combined Low Salt and Soft Diet—(Continued)

AFTERNOON

Fruit juice	1 4 oz glass

DINNER

Ground beef	3 ounces
Baked potato, no skin	1 whole
Beets, cooked	2 medium
Unsalted butter	1 pat
Unsalted white bread	1 slice
Fruit jello	½ cup
Milk	1 4-oz glass
Tea	1 cup
Sugar	2 teaspoons

LOW SODIUM DIETS

Several facts must be considered when a low sodium diet is ordered These diets must be followed rigidly if benefit is to result. They are difficult to maintain when the patient is not hospitalized. Since it is unpleasant to adhere strictly to a low salt regimen motivation must be stimulated in the patient. Low sodium diets can be made interesting and palatable if a certain amount of ingenuity is applied in their preparation

Before a low sodium diet is ordered, the physician must consider all of the facets of the case at hand in order to choose the diet which will be the most acceptable to the patient as well as the one which will produce the optimal benefits He may choose a diet of varying degrees of sodium restriction depending upon the severity of the manifestations and the environment of the patient. It must be kept in mind that it is impossible for patients who eat all their meals in restaurants and hotels to obtain unsalted food; moreover that the financially dependent patient will often be unwilling to add to his already overburdened budget the additional cost of special low salt preparations of foods.

Diets low in sodium are used most commonly in the following situations (1) in the treatment of congestive heart failure, (2) in the maintenance of compensation after recovery from congestive heart failure, (3) in the treatment of arterial hypertension, and (4) in the treatment of hypertensive cardiovascular disease before and after the onset of congestive manifestations.

General Considerations in the Use of the Low Sodium Regimen

In initiating a low sodium regimen practical problems often arise which may be difficult to solve One problem is that of the use of so-called "salt substitutes." Cardiac patients should be warned against the substitution of other salts for sodium chloride or ordinary table salt since certain of them have been found to be toxic Potassium and lithium salts are especially likely to give rise to toxicity. Calcium salts might give rise to toxicity in patients who are digitalized. In the long run I have found that it is better to have the patient adapt early to the lack of the flavor of salt in the diet. Vinegar, herbs, lemon juice, and salad oil may be used to add flavor White sugar, jams, jellies, honey, and homemade candies such as

As an interim step between the full liquid diet and the soft diet, the *modified* liquid diet would contain the full liquid constituents with the following supplements: soft-cooked eggs, refined cereals, plain or toasted white bread, butter, and simple puddings such as rice, tapioca, custard, and junket. These diets can be adjusted to the appropriate salt content.

SOFT DIET

A soft diet may be made as adequate in all of its components as a regular diet. In the soft diet, although the consistency of the food is changed, the amounts and variety remain sufficient to provide the necessary food essentials. The soft diet is easily digested, moderately low in residue, and served without spices or condiments. The regular soft diet is used when mechanical ease of eating and of digestion is the primary requirement. It contains the following foods

Milk, milk beverages, and cream
Egg (hard or soft-cooked, poached or scrambled)
Meat (ground or tender beef, lamb, veal), fish, poultry (without skin), broiled liver
Cheese (cottage or cream cheese)
Bread (plain or toasted, white, whole wheat, or fine rye without seeds), white crackers
Refined, enriched cereals, cereal products such as rice or noodles
Butter, fortified margarine, oil
Vegetables (pureed vegetables and those of low fiber content, cooked· asparagus, carrots, beets, spinach, squash, young peas and green beans, vegetable juices, and potatoes)
Cream soups strained, and broths
Fruits (cooked without skin or seeds, cooked puréed fruits, ripe banana, fruit juices)
Desserts such as simple puddings, plain cake, and frozen desserts without fruit or nuts
Tea, coffee, cocoa (as desired)

If a low salt, soft diet is required, the soft diet should be combined with the 2 0 or 3 0 Gm salt diet resulting in the following sample meal plan.

Combined Low Salt and Soft Diet

SAMPLE MENU

Food	*Amount*
BREAKFAST	
Orange juice	1 4 oz glass
Unsalted white toast	1 slice
Unsalted butter	1 pat
Unsalted cereal	½ cup
Milk	1 8 oz. glass
Sugar	2 teaspoons
LUNCHEON	
Egg, poached	1
Unsalted white toast	2 slices
Unsalted butter	1 pat
Carrots, cooked	½ cup
Canned peaches	2 halves
Milk	1 4-oz. glass
Tea	1 cup
Sugar	2 teaspoons

If the general low sodium diets which are adequate for normal nutrition are followed strictly, there is no need for additional vitamins. If the more restricted low sodium regimens which are known to be inadequate are followed for long periods of time, vitamin and mineral supplements should be prescribed.

Diets providing for restriction of the sodium intake which are in common use will now be described.

Rice Diet

The most drastic low sodium regimen is the rice diet initiated by Kempner for the treatment of hypertension and hypertensive cardiovascular disease. The diet contains only rice, fruit, fruit juice, and sugar. Since these foods are adequate only in calories, iron and vitamin supplements are required to make up these deficiencies. Kempner describes this regimen as follows:*

"The rice diet contains in 2000 calories not more than 5 Gm. of fat and about 20 Gm. of protein derived from rice and fruit and not more than 200 mg. of chloride and 150 mg. of sodium. A patient takes an average of 250 to 350 Gm. of rice (dry weight) daily, any kind of rice may be used provided no sodium chloride, milk, etc. has been added during its processing. The rice is boiled or steamed in plain water or fruit juice, without salt, milk or fat. If the sodium concentration of the plain water available is greater than 20 mg. per liter, distilled water should be used. All fruit juices and fruits are allowed, with the exception of nuts, dates, avocados, and any dried or canned fruit or fruit derivatives to which substances other than white sugar have been added. Not more than one banana a day should be taken. White sugar and dextrose may be used ad libitum; on an average a patient takes about 100 Gm. daily but, if necessary, as much as 500 Gm. daily should be used. Tomato and vegetable juices are not allowed. Usually no water is given and the fluid intake is limited to 700 to 1000 cc. of fruit juice per day. Supplementary vitamins are added in the following amounts: vitamin A 5000 units, vitamin D 1000 units, thiamin chloride 5 mg., riboflavin 5 mg., niacinamide 25 mg., calcium pantothenate 2 mg. No other medication is given unless it is specifically indicated."

Rice Diet

A MODEL MEAL PLAN FOR A RICE DIET CONTAINING 2000 CALORIES
(Servings are given in household measures)

Food	*Amount*
BREAKFAST	
Grapefruit juice	1 4-ounce glass
Applesauce, sweetened	1 saucedish
Puffed rice	¾ cup
with	
Sugar	1 tablespoon
and	
Pineapple juice	1 4 ounce glass

* Quoted from Kempner, Walter: Treatment of hypertensive vascular disease with rice diet. Am. J. Med. 4: 545, 1948.

peppermint patties (without salt) may be used to satisfy the desire for sweets. When desserts are allowed, cinnamon, or vanilla or lemon extract may be used. Paprika and curry, if desired, may be used for variety in flavors. Fruit juice or additional fruits may be taken between meals when appetite demands if fluids are not restricted. A cookbook for patients on low sodium diets has recently been published (Rice).

There are many sources of sodium of which one must be aware. Patients should be warned to read carefully the labels of products in order to omit those which include salt or other forms of sodium, such as sodium benzoate and baking powder in processing or flavoring Pretzels, olives, potato chips, pickles, ordinary baked goods, as well as most candies and nut bars, are common articles which must be avoided by patients on low salt diets.

In prescribing sodium-restricted diets the composition of water used in cooking and preparing beverages must be taken into consideration,* as the sodium content of the drinking water is high in some places. Water which has been treated for "water softening" contains added sodium. Patients should also be warned against the use of soda or soda products, waters carbonated with sodium bicarbonate, and mineral waters containing sodium

The sodium content of *medications* should be checked. Sodium bicarbonate should not be prescribed for indigestion and sodium salts should not be used for other purposes without due consideration Bismuth, calcium, and magnesium salts, and aluminum hydroxide can be used for antacids. Saline cathartics and laxatives which contain sodium salts should be avoided; epsom salts and milk of magnesia can be substituted Many patent remedies contain sodium, and should not be used by patients on low salt diets.

Salt-free or "sweet" butter is readily obtained at most stores where dairy products are sold Many large bakeries are making unsalted bread because of the recent increase in demand, it is also made by health food baking companies in the larger cities which will send it via parcel post on patients' orders. Salt-free bread and rolls can be made in the home by substituting Lonalac** for milk and omitting salt and baking powder.

Low salt diets are unpleasant for patients who are accustomed to using large amounts of *milk* One quart of milk contains 480 mg. of sodium or 1.2 Gm. of salt. Several manufacturers make low sodium milk, and such products must be utilized in low salt diets if protein, minerals, and vitamins are to be maintained at adequate levels Lonalac has been used in the menus illustrated in this chapter because of ease of preparation, availability, and palatability of the product. Other forms of low sodium, high protein supplements are Delcos,† Somagen,‡ and Protinal § Sometimes the sodium chloride is eliminated from the milk by dialysis.

Eggs and meat are also high in natural salt and may be eaten only in limited amounts A few low sodium meats are now available.¶

* [illegible] supplies may be obtained from Research [illegible]

** [illegible]

§ [illegible]

¶ Armour and Company.

Foods to Omit

Milk and milk products, except Lonalac as allowed
Salt and all foods prepared or preserved with it
Cured meats (ham, bacon, sausage), and fish if processed with brine (this often includes frozen fish)
Cereals except those made without salt
Salted butter, salted mayonnaise, salted French dressing
The following vegetables: beets, kale, swisschard, spinach frozen peas, frozen lima beans, all commercially canned vegetables and legumes
All cheeses except unsalted pot cheese
Salted nuts, salted crackers, salted broths
Condiments (catsup, prepared mustard, chili sauce, and celery or onion salt)

0.5 to 1.0 Gm. Low Salt Diet (200 to 400 mg Sodium)

SAMPLE MENU

Food	*Amount*
BREAKFAST	
Orange juice	1 4-ounce glass
Cereal, unsalted	¾ cup
Cream	2 ounces
Sugar	1 tablespoon
Egg	1
Unsalted toast	1 slice
Unsalted butter	1 pat
Coffee	1 cup
LUNCH	
Grapefruit	½
Baked potato	1 whole
Squash, baked	½
Lettuce and tomato salad	1 tomato, 2 leaves lettuce
Unsalted French dressing	1 tablespoon
Unsalted bread	2 slices
Unsalted butter	1 pat
Canned pears	2 halves
Lonalac	1 glass
Tea	1 cup
Sugar	1 tablespoon
DINNER	
Pineapple juice	1 4 ounce glass
Roast lamb	3 ounces
Potato	1 small
Fresh peas	½ cup
Unsalted bread	1 slice
Unsalted butter	1 pat
Stewed apples	½ cup
Lonalac	1 glass
Coffee	1 cup
Sugar	1 tablespoon

Rice Diet—(*Continued*)

LUNCHEON	
Grape juice	1 8 ounce glass
Rice baked with fresh tomatoes	¾ cup (3 tbsp. dry)
Pear	2 halves
baked with	
Sugar	2 tablespoons
AFTERNOON	
Citrus fruit juice	1 8-ounce glass
DINNER	
Orange and cranberry juice	1 8-ounce glass
Rice	¾ cup (3 tbsp. dry)
baked with	
Canned pineapple	2 slices
and	
Sugar	2 tablepsoons
Sliced tomato	1 whole
Fruit plate:	
Sliced banana	½
Apple	½
Grapefruit sections	6
Whole grapes	12–15
EVENING	
Apple juice	1 8-ounce glass

The fruits in the rice diet may be served raw or cooked, and with or without sugar. The rice may be steamed, boiled, or boiled and then baked. *No table salt* is to be used in the preparation of any part of the diet. *Nothing* is to be taken except the fruit, rice, sugar, and fruit juice as allowed.

Low Salt Diet—0.5 to 1.0 Gm. (200 to 400 mg. Sodium)

The most limited of the low sodium diets which are adequate for normal nutrition, without vitamin and mineral supplements, is the 0.5 to 1.0 Gm. salt (200 to 400 mg. sodium) regimen. The protein foods (meat, eggs, and milk) have a relatively high sodium content and therefore must be replaced in the low salt diet by low sodium foods of equal nutritional value. The following is a sample of the 200 to 400 mg. sodium diet making use of Lonalac.

Foods for the Day	*Amount*
	1
	3 ounces
	1 pint
Butter (unsalted)	3 pats
Bread (unsalted)	4 slices
Cereal (made without salt)	¾ cup
Vegetables (prepared without salt)	4 servings
Potato	1
Fruits (canned, fresh, or stewed)	4–5 servings
Sugar (white)	3–4 tablespoons
Cream	2 ounces

2.0 Gm. Low Salt Diet (800 mg. Sodium)—(*Continued*)

DINNER

Pineapple juice	1 4 ounce glass
Roast lamb	3 ounces
Squash, baked	½
Broccoli	3 stalks
Unsalted bread	1 slice
Butter	1 pat
Sliced bananas and oranges	½ cup
Sugar	1 tablespoon
Coffee	1 cup
Milk	1 glass

Low Salt Diet—3.0 Gm. (1.2 Gm. Sodium)

The 1.0 and 2.0 Gm. salt (400 and 800 mg. sodium) diets provide only fruit for desserts. The addition of sodium that results from the use of soda, baking powders, condiments, and spices in other desserts makes it impossible to include them. The addition of one dessert daily (other than fruit) will add approximately 1.0 Gm. salt (400 mg. sodium) to the diet. The 3.0 Gm. salt or 1.2 Gm. sodium diet, then, is the same as the 2.0 Gm. salt (or 800 mg. sodium) with the addition of one dessert daily. If preferred, particularly in diets ordered for men, four ounces of meat may be added to the diet in place of dessert.

3.0 Gm. Low Salt Diet (1.2 Gm. Sodium)

SAMPLE MENU

Food	*Amount*
BREAKFAST	
Orange juice	1 4-ounce glass
Oatmeal, unsalted	¾ cup, cooked
Cream	2 ounces
Sugar	2 tablespoons
Unsalted toast	1 slice
Butter	1 pat
Coffee	1 cup
LUNCHEON	
Pineapple juice	1 4-ounce glass
Egg	1
Asparagus with lemon juice	6 stalks
Unsalted bread	2 slices
Butter	1 pat
Fruit cup of sliced oranges and bananas	½ cup
Milk	1 glass

Low Salt Diet—2.0 Gm. (800 mg. Sodium)

Slightly more palatable is the 2.0 Gm. salt or 800 mg. sodium diet, since one pint of milk replaces the Lonalac, and regular butter or fortified oleomargarine may be used.

Foods to Use Daily	*Amount*
Egg	1
Meat, unsalted fish, or poultry	3 ounces
Milk	1 pint
Cream	2 ounces
Butter or oleomargarine	3 pats
Cereal, unsalted	¾ cup
Bread, unsalted	4 slices
Potato or substitute	1 serving
Vegetables	4 servings
Fruit	4–5 servings
Sugar	3 tablespoons

Foods to Omit

Salt and all foods prepared or preserved with it
Cured meats(ham, bacon, sausage), fish if processed with brine (this often includes frozen fish)
Cereals except those made without salt
Salted mayonnaise, salted French dressing
The following vegetables beets, kale, swisschard, spinach, frozen peas, frozen lima beans commercially canned vegetables and legumes
All cheeses except unsalted pot cheese
Salted nuts, salted crackers, salted broths
Condiments (catsup, prepared mustard, chili sauce, and celery or onion salt)

2.0 Gm. Low Salt Diet (800 mg. Sodium)

Sample Menu

Food	*Amount*
BREAKFAST	
Orange juice	1 4 ounce glass
Oatmeal, unsalted	¾ cup cooked
Cream	2 ounces
Sugar	2 tablespoons
Unsalted toast	1 slice
Butter	1 pat
Coffee	1 cup
LUNCHEON	
Egg	1
Potato	1 whole
Lettuce and tomato salad	1 whole tomato, 2 leaves lettuce
Bread, unsalted	2 slices
Butter	1 pat
Canned pears	2 halves
Milk	1 glass

5.0 Gm. Low Salt Diet (2.0 Gm. Sodium)—(Continued)

LUNCHEON

Roast beef	3 ounces
Squash, baked	½
Asparagus	6 stalks
Whole wheat roll	1 roll
Butter	1 pat
Sliced banana	1
Milk	1 glass

DINNER

Lamb chop	1 (3 ounces)
Potato	1
Peas, fresh	½ cup
Fruit salad	1 small
Whole wheat bread	1 slice
Butter	1 pat
Apple pie	1 slice
Coffee	1 cup
Milk	1 glass
Sugar	1 teaspoon

For moderate salt restriction, the above is the most workable diet for use with ambulatory patients since it is essentially a normal diet with approximately 2.0 to 3.0 Gm. of salt added in preparation. It is especially useful in the case of the patient who customarily adds large amounts of salt to his regular diet or is especially fond of highly seasoned and salted foods. It should not be referred to erroneously, as it often is, as a "salt-free diet."

Low Salt—High Protein Diet

A diet extremely low in sodium and high in protein is often desirable for patients with heart failure in whom the serum protein is low It is difficult to attain since foods high in protein also contain the most liberal amounts of sodium. By using low sodium substitutes for milk, such as Lonalac or Somagen, it is possible to provide 120 Gm of protein and reduce the sodium content to 400 mg in the diet which follows:

Foods for the Day

Food	*Amount*
Eggs	2
Unsalted meat, fish, chicken	6 ounces
Lonalac	5 glasses
Cream	¼ cup or 1 2 ounce glass
Unsalted butter	As desired
Unsalted bread	5 slices
Unsalted cereal	¾ cup
Potato or substitute	2 servings
Two other vegetables (omit those high in sodium)	2 servings
Fresh or stewed fruit	4 servings
Sugar	As desired

3.0 Gm. Low Salt Diet—(Continued)

DINNER

Roast lamb	3 ounces
Potato, Baked	1 whole
Squash, baked	½
Salad of lettuce and tomato	1 tomato, 2 leaves lettuce
Bread, unsalted	1 slice
Butter	1 pat
Apple pie	1 serving
Milk	1 glass
Coffee	1 cup
Sugar	1 tablespoon

Low Salt Diet—5.0 Gm. (2.0 Gm. Sodium)

The simplest of the low sodium diets is the 5.0 Gm. salt diet. This is a norma diet in respect to the amount of salt used in cooking but no salt is served on th tray or added at the table.

Foods Allowed Daily	*Amount*
Eggs	1
Meat, unsalted fish, or poultry	6 ounces (2 servings)
Milk	1 pint
Cream	2 ounces
Butter or oleomargarine	3 pats
Bread, whole grain	4 slices
Cereal	¾ cup
Potato	1
Vegetables	As desired
Fruits	As desired
Dessert	One daily other than fruit
Sugar	As desired

Foods to Be Omitted

Cured meats and fish (ham, bacon, sausage, sardines)
Salted mayonnaise, French dressing
Cheeses except unsalted pot cheese
Salted nuts, salted crackers, salted broth, canned soups, condiments such as catsup, chili sauce, steak sauces, and celery or onion salt
Salt added after cooking

5.0 Gm. Low Salt Diet (2.0 Gm. Sodium)

SAMPLE MENU

Food	*Amount*
BREAKFAST	
Orange juice	1 4 ounce glass
Egg	1
Oatmeal	¾ cup
Cream	2 ounces
Sugar	2 tablespoons
Whole wheat bread	1 slice
Butter	1 pat
	1 cup

The sodium chloride content of the 800 cc of milk would be 1.0 Gm. (or 400 mg sodium), the caloric value around 545.

Schemm Regimen

The Schemm regimen, consisting of a low sodium, acid ash diet with the forcing of a large fluid intake,* was thought by its originator to be especially effective in the mobilization of fluids in patients suffering marked congestive heart failure. Although this regimen has been tried by many observers, I am not aware that it is now being used to any great extent We were unable to free patients of signs and symptoms of heart failure by this regimen.† Mercurial diuretics were also required to increase the output of urine, but even these, in the face of the large fluid intake, were inadequate to bring about restoration of compensation We concluded that restriction of fluid is required as an integral part of a regimen designed for the most effective elimination of fluid accumulations in congestive heart failure

In the Schemm regimen the diet is constructed so that it yields an acid ash In order to insure an acid urine two devices were used by Schemm (1) Ammonium chloride (itself having diuretic properties) was given orally daily, (2) a few drops of dilute hydrochloric acid were added to each glass of water the patient drank. The fluid intake was pushed to 3000 to 7000 cc a day, the majority of patients taking approximately 5000 cc daily When this amount of fluid could not be taken orally Schemm recommended that it be given parenterally even though the patient suffered congestive heart failure

We found that patients objected to drinking such large quantities of water and to the monotony of the diet They preferred a regular low salt diet with fluid restriction, to the regimen outlined by Schemm

REDUCING DIETS

General Consideration

We are not concerned in this chapter with the etiology of obesity but only with its effects on the patient with heart disease The death rate from heart disease of overweight individuals is greater than of those of average weight and of those who are underweight, the more overweight the subject the greater the mortality. This provides ample reason for insistence on weight reduction in order to lessen the load on the heart and to increase the reserve power of the heart. Tables IX-A and IX-B provide satisfactory estimates of the ideal weights of adults over 25 years of age.

Restoration to an ideal weight is indicated for all individuals whether or not they have a cardiac disorder It is, however, especially important for patients with organic heart disease, patients with heart failure, patients in the older age group, those with coronary artery disease with angina, those who have suffered myocardial infarction, and those with arterial hypertension or hypertensive cardiovascular disease.

* Schemm, F R A high fluid intake in the management of edema, especially cardiac edema I The details and basis of the régime Ann Int Med 17 952, 1942

† Newman, A A, and Stewart, H J Experience with the Schemm regimen in the treatment of congestive heart failure. Ann Int Med 28 916, 1948

Low Salt—High Protein Diet (400 mg. Sodium)

Sample Menu

Food	*Amount*
BREAKFAST	
Fruit juice	1 4-ounce glass
Eggs, poached	2
Unsalted bread toasted	1 slice
Unsalted butter	2 pats
Coffee	1 cup
Unsalted cereal	¾ cup
Cream	¼ cup
Sugar	As desired
MID-MORNING	
Lonalac	1 8 ounce glass
LUNCHEON	
Unsalted roast lamb	3 ounces
Unsalted potato, baked	1 medium
Unsalted fresh tomato, broiled	1 whole
Unsalted bread	2 slices
Unsalted butter	2 pats
Fruit cup	½ cup
Lonalac	1 8 ounce glass
AFTERNOON	
Lonalac, fruit flavored	1 8 ounce glass
DINNER	
Fruit juice cocktail	½ cup
Broiled chicken, sliced	3 ounces
Steamed rice	½ cup
Tossed salad with oil and lemon	½ cup
Unsalted bread	2 slices
Unsalted butter	2 pats
Lonalac	1 8-ounce glass
Stewed apricots	4 to 6 halves
EVENING	
Lonalac, vanilla flavored	1 8-ounce glass

Karell Diet

This diet may be prescribed for a short time for patients with congestive heart failure. It provides for low salt and restricted fluid intake, but is deficient in calories It is an inadequate diet and should be used for only a few days. In its strict form, a total of 800 cc. of milk is given in 24 hours. This is divided into four feedings of 200 cc. each at 8 A.M., 12 Noon, 4 P.M., and 8 P.M. It provides an easy way to take care of the low salt and restricted fluid intake, but is unpalatable to sick patients and I rarely use it. It is much more satisfactory to give a low salt diet of more palatable foods, and to allow the fluid intake in the form of water and fruit juices.

As a starting point the total caloric intake of the patient is reduced to approximately 50 per cent of the total energy requirement. This necessitates the use of the patient's own body fat. It is important to note that the *caloric intake only* is reduced. Due regard must be given to maintenance of adequate protein, mineral, and vitamin contents of the diet. Overweight individuals need these dietary constituents in the required amounts if they are to maintain good health.

The need for cooperation by the patient in carrying out the dietary regimen must not be underestimated. If results of lasting significance are to be obtained, any concurrent emotional factors must be considered and dealt with. The patient should have adequate explanation of the reasons for the diet, the objectives which are to be accomplished, and his part in carrying out the actual restrictions. As the patient progresses he should have regular check-ups to discuss his improvement. Reassurance and encouragement prove invaluable aids in providing an incentive. It is rare that a patient who is merely "presented" with a diet list and told to "follow it" has the moral stamina or self-control to adhere to the diet without at least a spark of stimulation from the physician and the dietitian. The weight reduction should be followed so that when the optimal weight has been attained the diet can be appropriately altered. Once the surplus fat has been burned, the caloric intake must now be adjusted to the requirements of the individual.

The caloric requirement or energy needs of the average man engaging in moderate activity has been set by the National Research Council at 3000 calories daily. The reduction of this estimate by 50 per cent would result in a 1500-calorie diet, which should be sufficient to achieve an average weight loss of approximately two pounds of fat per week. For the average woman, whose caloric requirement is estimated at 2400 calories per day, a 1200-calorie diet should bring about the same results.

The 1200- and 1500-calorie diets meet all the nutritional requirements except, of course, the requirement for calories. Occasionally even lower amounts of calories are required in order to bring about loss of weight. Diets restricted to 600 or 800 calories are not adequate for normal nutrition, accordingly vitamin supplements, particularly vitamin A, thiamin, and niacin must be added.

Without Salt Restriction

Samples of 1500- and 1200-calorie diets in which salt restriction is not required are as follows:

Outline for an Adequate 1500-Calorie Diet

Foods for the Day	*Amount*
Egg, not fried	1
Meat, fish, or poultry, lean	5 ounces
Milk	1 pint
Butter or oleomargarine	3 pats
Group I vegetable*	2 servings
Group II vegetables*	1 serving
Potato or Group III vegetable*	1 serving
Fruits as listed*	3 servings
Bread, whole grain, preferred	3 slices
Coffee, tea, clear broth	As desired

* See Table X, page 570

Table IXa. Ideal Weights for Men*

(Ages Twenty-five and Over)

Height (With shoes)		*Weight in pounds* (As ordinarily dressed)		
Feet	Inches	Small frame	Medium frame	Large frame
5	2	116 25	124-33	131-42
5	3	119-28	127-36	133-44
5	4	122-32	130 40	137-49
5	5	126-36	134-44	141-53
5	6	129-39	137-47	145-57
5	7	133-43	141-51	149-62
5	8	136-47	145-56	153-66
5	9	140-51	149 60	157-70
5	10	144-55	153-64	161-75
5	11	148-59	157-68	165 80
6	0	152-64	161-73	169 85
6	1	157-69	166 78	174 90
6	2	163-75	171-84	179-96
6	3	168-80	176-89	184-202

* Figures from Metropolitan Life Insurance Company, Statistical Bureau, 1943.

Table IXb. Ideal Weights for Women*

(Ages Twenty five and Over)

Height (With shoes)		*Weight in pounds* (As ordinarily dressed)		
Feet	Inches	Small frame	Medium frame	Large frame
4	11	104-11	110-18	117 27
5	0	105-13	112-20	119-29
5	1	107-15	114-22	121-31
5	2	110 18	117-25	124-35
5	3	113-21	120-28	127-38
5	4	116-25	124 32	131-42
5	5	119-28	127-35	133 45
5	6	123-32	130 40	138-50
5	7	126-36	134-44	142-54
5	8	129-39	137-47	145-58
5	9	133 43	141-51	149-62
5	10	136-47	145-55	152-66
5	11	139-50	148 58	155-69
5				

* Figures from Metropolitan Life Insurance Company, Statistical Bureau, 1943

1200-Calorie Diet

Sample Menu

Food	*Amount*
BREAKFAST	
Orange juice	1 4 ounce glass
Boiled egg	1
Whole wheat or enriched bread (toast)	1 slice
Butter	½ pat
Milk	1 4 ounce glass
Coffee	1 cup
LUNCHEON	
Sliced chicken	2 ounces
Broiled or sliced tomato	1 serving
Broccoli with lemon	1 serving
Rye bread	½ slice
Butter	½ pat
Tangerines	2 medium
Milk	1 8 ounce glass
DINNER	
Beef patty	2 ounces
Spinach	1 serving
Carrots	1 serving
Rye bread	½ slice
Butter	½ pat
Grapefruit	½
Milk	1 4 ounce glass
Coffee or tea	If desired

Only the foods listed on the foregoing reducing diets above should be used There are some foods which are so high in fats and carbohydrates that they must be eliminated completely from the low-calorie regimen. Although negative teaching should for psychologic reasons follow the positive teaching, the foods to avoid should always be pointed out to patients initiating a reducing routine

Foods to Omit on the 1200- and 1500-Calorie Diets

Sugar, jelly, honey, candies, nuts, chocolate, dried fruits, desserts (pies, cakes, cookies, puddings, jello, ice cream)
Fat meats (pork, ham, bacon, sausage, duck, fish canned in oil)
Fried foods, gravies, sauces, cream (sweet and sour), oil, oil dressings, mayonnaise
Soda pop and soft drinks, beer, and wine

Alcoholic beverages, although they contain no actual food value, supply energy to the body through oxidation of the alcohol. Because of the calories which would be added to the diet, it is obvious that the patient on a reducing regimen must be warned against the use of cocktails or highballs to excess

Saccharin or Sucaryl* may be used in place of sugar for sweetening beverages or

* Abbott Laboratories.

1500-Calorie Diet

Sample Menu

Food	Amount
BREAKFAST	
Orange juice	1 4 ounce glass
Poached egg	1
Whole wheat toast	1 slice
Butter	1 pat
Coffee	1 cup
Milk	1 4 ounce glass
LUNCHEON	
Sliced pot roast	2 ounces
Spinach or lettuce and tomatoes	1 serving
Carrots	1 serving
Rye bread	1 slice
Butter	1 pat
Fruit cup	1 serving, mixed
Milk	1 8 ounce glass
Coffee or tea	If desired
DINNER	
Consommé	If desired
Veal chop	3 ounces
Boiled potato	*1 serving*
Asparagus	1 serving
Cracked wheat bread	1 slice
Butter	1 pat
Sliced banana	½
Milk	1 4 ounce glass
Coffee or tea	If desired

Outline of Adequate Diet of 1200 Calories

Foods for the Day	*Amount*
Egg, not fried	1
Meat, fish, or poultry, lean	4 ounces
Milk	*1 pint*
Butter or oleomargarine	1½ pats
Group I vegetables*	3 servings
Group II vegetables*	1 serving
Fruits, as listed*	3 servings
Bread, whole grain preferred	2 slices
Coffee, tea, clear broth	As desired

* See Table X, p 570

foods without any untoward effects on the patient or without unbalancing the diet Sucaryl contains sodium and cannot be used in low sodium regimens. Foods may also be made more palatable by the use of lemon juice, vinegar, salt (if not contraindicated), pepper, and other spices.

Low Salt Reducing Diet

Occasionally, particularly in the case of hypertensive patients, a reducing diet of low sodium content is required

Low Salt, Reducing Diet (1200 Calories, Less than 1 0 Gm Salt)

Foods for the Day	*Amount*
Egg (not fried)	1
Meat, unsalted fish, or chicken	1 3-ounce serving
Milk	1 pint
Unsalted butter	1½ pats
Unsalted cereal	½ cup
Unsalted bread	2 slices
Group I vegetable*	1 serving
Group II vegetable*	1 serving
Potato or Group III vegetable*	1 serving
Fruit, as listed	3 servings
Coffee or tea	As desired

*Refer to table X

The same vegetables are omitted from this diet as on the regular 1 0-Gm salt diet, and in addition foods high in carbohydrate and fat are omitted All cooking is done without salt or sugar, but pepper, vinegar, lemon, herbs, onions, leeks, and saccharin may be used for flavoring Broths are not allowed and carbonated water may not be used

LOW CHOLESTEROL DIET

The low cholesterol diet is one in which the fats are reduced to a minimum. Recent evidence indicates that the total fat content of the diet is more important in altering serum cholesterol than is the amount of cholesterol ingested. Since a low fat diet automatically restricts cholesterol ingestion, the serum cholesterol may fall on a diet of 60 Gm of fat in one individual, while one restricted to 20 Gm. may be required in another. Effectiveness of the diet can be measured by serial determinations of serum cholesterol The usual practice is to start patients on a 25 to 30 Gm. fat diet When the diet goes below this amount of fat, vitamin supplements should be added to replace the fat-soluble vitamins if the patient is not to be subject to vitamin deficiency. The Kempner "rice diet" is cholesterol free and contains only 5 Gm of fat In order that the total daily cholesterol intake shall not exceed 25 to 30 Gm, the high fat foods are limited as follows.

Whole eggs	One per oz as meat substitute
Meat, fish, poultry	3 ounces daily
Milk, skimmed only	1 quart daily
Butter or oleomargerine	2 pats

Table X. Group Classification of Fruits and Vegetables

Vegetables

Group I

Vegetable	*1 serving equals*
Asparagus	*6 stalks*
Beans, string	½ cup
Beet greens	½ cup
Broccoli	6 stalks
Cabbage, raw	1½ cups
Cabbage, cooked	½ cup
Cauliflower	½ cup
Celery, raw	4 stalks
Celery, cooked	½ cup
Chard leaves	½ cup
Cucumbers	½ medium
Lettuce, head	¼ head
Lettuce, leaf	10 leaves
Mustard greens	½ cup
Radishes	10
Sauerkraut	½ cup
Spinach	½ cup
Squash, summer	½ cup
Tomatoes, canned	½ cup
Tomato, fresh	1 medium
Tomato juice	½ cup
Turnip tops	½ cup

Group II

Vegetable	*1 serving equals*
Beets	*2 medium*
Brussels sprouts	½ cup
Carrots	½ cup
Dandelion greens	½ cup
Eggplant	½ cup
Kohlrabi	½ cup
Okra	½ cup
Onions	2 medium
Parsnips	1 medium
Peas	½ cup
Pepper, green	1 large
Pumpkin	½ cup
Rutabagas	½ cup
Squash, winter	½ cup
Turnips	½ cup

Group III

Vegetable	*1 serving equals*
Beans, lima	½ cup
Beans, kidney	½ cup
Corn, canned	½ cup
Corn, fresh	1 medium ear
Hominy, canned	*¾ cup*
Potato, white	1 small
Potato, sweet	½ cup

Fruits (fresh or cooked without sugar)

Fruit	*1 serving equals*
Apple	½ medium
Apricot	2 medium
Banana	*½ small*
Blackberries	½ cup
Blueberries	½ cup
Cantaloupe	½ medium
Cherries, sweet	10
Grapefruit	½ medium
Grapefruit juice (unsweetened)	½ cup
Grapes	15-20

Fruit	*1 serving equals*
Orange	1 medium
Orange juice	½ cup
Peaches	1 whole
Pears	½ medium
Pineapple	1 medium slice
Pineapple juice (unsweetened)	½ cup
Plums	3 medium
Raspberries	1 cup
Strawberries	1 cup
Tangerines	2 medium
Watermelon	1 slice

following regimen restricting foods of 0.05 mg per cent or more in purine content is adequate for normal nutrition.

Foods Omitted

Glandular meats and meat products, meat broths, and gravies Vegetables as follows. asparagus, dried beans, lentils, mushrooms, peas, and spinach.

Foods Restricted

Meats, fish, poultry	2 ounces daily
Coffee, tea, cocoa	1 cup daily

Caffeine is, chemically speaking, in the purine group. Even though it is probably not convertible into uric acid, most investigators agree that it should be omitted from the diet. There are many beverages which may be served hot (Sanka, Postum, Ovaltine) which contain no caffeine and may be substituted for coffee and tea Alcoholic beverages are thought to be harmful although small amounts if well diluted are sometimes allowed Restriction of foods containing purine derivatives is indicated in patients who have a high level of blood uric acid.

Low Purine Diet

Sample Menu

Food	*Amount*
BREAKFAST	
Orange juice	1 4 ounce glass
Oatmeal	¾ cup
Whole wheat toast	2 slices
Butter	2 pats
Cream	2 ounces
Sugar	1 tablespoon
Sanka coffee	1 cup
Milk	1 glass
LUNCHEON	
Cream of corn	½ cup
Plain omelet	2 eggs
Grilled tomato	1 whole
Head lettuce	¼ head
Hard roll	1
Butter	1 pat
Milk	1 glass
Fruit cup	½ cup
DINNER	
Pineapple juice	1 4 ounce glass
Sliced chicken	2 ounces
Candied sweet potato	1
Beets	2 medium
Whole wheat bread	1 slice
Butter	1 pat
Milk	1 glass
Orange tapioca pudding	½ cup
EVENING	
Milk	1 glass

Cheese, except that made with skimmed milk, is not permitted. Desserts should be limited to fruits, puddings made with skimmed milk, gelatin, fruit ices, and angel food cake. Sugar, jelly, jams, and honey may be used as desired. Fruits and vegetables also are used as desired but they should be prepared without extra butter or cream

Low Cholesterol Diet (25 Gm. Fat)

SAMPLE MENU

Food	*Amount*
BREAKFAST	
Orange juice	1 4 ounce glass
Oatmeal	¾ cup
Sugar	1 tablespoon
Skimmed milk	1 glass
Toast	1 slice
Oleomargarine or butter	1 teaspoon
Coffee	1 cup
LUNCHEON	
Pot cheese	½ cup
Vegetable plate	
Baked potato	1
Grilled tomato	1 whole
Kernel corn	½ cup
Fresh fruit salad	1 serving
Bread or roll	1 slice
Oleomargarine or butter	2 teaspoons
Fruit jello	1 serving
Skimmed milk	1 glass
DINNER	
Tomato juice	1 4 ounce glass
Grilled round steak	1 3 ounce serving
Lima beans	½ cup
Glazed carrots	½ cup
Roll	1
Oleomargarine or butter	2 teaspoons
Stewed peaches	½ cup
Skimmed milk	1 glass
EVENING	
Skimmed milk or buttermilk	1 glass

Restriction of cholesterol in the diet should be undertaken if repeated estimations of the serum cholesterol show significant elevations in the absence of myxedema. It is not yet known whether reduction in cholesterol in the diet will prevent or delay the progress of arteriosclerosis, or alleviate its effects once the process has been initiated.

LOW PURINE DIET

The normal diet is said to contain 600 to 1000 mg of purine For a low purine diet to be effective the purine content should be reduced to 100 to 150 mg. The

following regimen restricting foods of 0.05 mg. per cent or more in purine content is adequate for normal nutrition

FOODS OMITTED

Glandular meats and meat products, meat broths, and gravies Vegetables as follows asparagus, dried beans, lentils, mushrooms, peas, and spinach

FOODS RESTRICTED

Meats, fish, poultry	2 ounces daily
Coffee, tea, cocoa	1 cup daily

Caffeine is, chemically speaking, in the purine group Even though it is probably not convertible into uric acid, most investigators agree that it should be omitted from the diet. There are many beverages which may be served hot (Sanka, Postum, Ovaltine) which contain no caffeine and may be substituted for coffee and tea. Alcoholic beverages are thought to be harmful although small amounts if well diluted are sometimes allowed. Restriction of foods containing purine derivatives is indicated in patients who have a high level of blood uric acid.

Low Purine Diet

SAMPLE MENU

Food	*Amount*
BREAKFAST	
Orange juice	1 4 ounce glass
Oatmeal	¾ cup
Whole wheat toast	2 slices
Butter	2 pats
Cream	2 ounces
Sugar	1 tablespoon
Sanka coffee	1 cup
Milk	1 glass
LUNCHEON	
Cream of corn	½ cup
Plain omelet	2 eggs
Grilled tomato	1 whole
Head lettuce	¼ head
Hard roll	1
Butter	1 pat
Milk	1 glass
Fruit cup	½ cup
DINNER	
Pineapple juice	1 4-ounce glass
Sliced chicken	2 ounces
Candied sweet potato	1
Beets	2 medium
Whole wheat bread	1 slice
Butter	1 pat
Milk	1 glass
Orange tapioca pudding	½ cup
EVENING	
Milk	1 glass

Cheese, except that made with skimmed milk, is not permitted. Desserts should be limited to fruits, puddings made with skimmed milk, gelatin, fruit ices, and angel food cake. Sugar, jelly, jams, and honey may be used as desired Fruits and vegetables also are used as desired but they should be prepared without extra butter or cream

Low Cholesterol Diet (25 Gm. Fat)

SAMPLE MENU

Food	*Amount*
BREAKFAST	
Orange juice	1 4-ounce glass
Oatmeal	3/4 cup
Sugar	1 tablespoon
Skimmed milk	1 glass
Toast	1 slice
Oleomargarine or butter	1 teaspoon
Coffee	1 cup
LUNCHEON	
Pot cheese	1/2 cup
Vegetable plate:	
Baked potato	1
Grilled tomato	1 whole
Kernel corn	1/2 cup
Fresh fruit salad	1 serving
Bread or roll	1 slice
Oleomargarine or butter	2 teaspoons
Fruit jello	1 serving
Skimmed milk	1 glass
DINNER	
Tomato juice	1 4-ounce glass
Grilled round steak	1 3 ounce serving
Lima beans	1/2 cup
Glazed carrots	1/2 cup
Roll	1
Oleomargarine or butter	2 teaspoons
Stewed peaches	1/2 cup
Skimmed milk	1 glass
EVENING	
Skimmed milk or buttermilk	1 glass

Restriction of cholesterol in the diet should be undertaken if repeated estimations of the serum cholesterol show significant elevations in the absence of myxedema. It is not yet known whether reduction in cholesterol in the diet will prevent or delay the progress of arteriosclerosis, or alleviate its effects once the process has been initiated.

LOW PURINE DIET

The normal diet is said to contain 600 to 1000 mg. of purine. For a low purine diet to be effective the purine content should be reduced to 100 to 150 mg. The

following regimen restricting foods of 0.05 mg. per cent or more in purine content is adequate for normal nutrition.

Foods Omitted

Glandular meats and meat products, meat broths, and gravies Vegetables as follows: asparagus, dried beans, lentils, mushrooms, peas, and spinach

Foods Restricted

Meats, fish, poultry	2 ounces daily
Coffee, tea, cocoa	1 cup daily

Caffeine is, chemically speaking, in the purine group. Even though it is probably not convertible into uric acid, most investigators agree that it should be omitted from the diet. There are many beverages which may be served hot (Sanka, Postum, Ovaltine) which contain no caffeine and may be substituted for coffee and tea. Alcoholic beverages are thought to be harmful although small amounts if well diluted are sometimes allowed. Restriction of foods containing purine derivatives is indicated in patients who have a high level of blood uric acid

Low Purine Diet

Sample Menu

Food	*Amount*
BREAKFAST	
Orange juice	1 4 ounce glass
Oatmeal	¾ cup
Whole wheat toast	2 slices
Butter	2 pats
Cream	2 ounces
Sugar	1 tablespoon
Sanka coffee	1 cup
Milk	1 glass
LUNCHEON	
Cream of corn	½ cup
Plain omelet	2 eggs
Grilled tomato	1 whole
Head lettuce	¼ head
Hard roll	1
Butter	1 pat
Milk	1 glass
Fruit cup	½ cup
DINNER	
Pineapple juice	1 4 ounce glass
Sliced chicken	2 ounces
Candied sweet potato	1
Beets	2 medium
Whole wheat bread	1 slice
Butter	1 pat
Milk	1 glass
Orange tapioca pudding	½ cup
EVENING	
Milk	1 glass

Very often the low purine diet must be combined with the reducing regimen for patients who are obese. The same restrictions are enforced concerning the foods high in purine but in addition, foods normally omitted from the reducing regimen are not allowed. The following is a typical plan for a 1200-calorie, low purine diet.

1200-Calorie—Low Purine Diet

Foods Allowed Daily	*Amount*
Egg	1
Lean meat, fish, poultry	1 2 ounce serving
Milk	3 glasses
or	
Milk	2 glasses
and	
Cheese, firm type	1 ounce
Butter or oleomargarine	1½ pats
Bread, whole grain preferred	2 slices
Cereal, whole grain preferred	½ cup cooked
Vegetables Group I*	3 servings
Vegetables Group II*	1 serving
Fruits from group	3 servings
Regular coffee (Sanka as desired) or tea	1 cup

* Table X, page 570

Sample Menu

Food	*Amount*
BREAKFAST	
Orange juice	1 4 ounce glass
Oatmeal	½ cup, cooked
with	
Milk	1 8 ounce glass
Whole wheat toast	1 slice
Butter	½ pat
Sanka coffee	1 cup
LUNCHEON	
Egg, hard cooked	1
Lettuce and tomato salad	2 leaves, 1 whole tomato
Rye bread	1 slice
Butter	½ pat
Sliced orange	1 whole
Milk	1 glass
DINNER	
Roast beef	2 ounces
Sliced cucumber and lettuce	1 whole, medium, 2 leaves
Sliced carrots	1 serving
Chopped spinach	1 serving
Butter	½ pat
Grapefruit	½
Milk	1 glass

WEIGHT-GAINING DIETS

High Caloric Diet

The high caloric diet is used when patients are underweight, or whose metabolic needs are increased. Such a diet includes all the foods in the normal diet with the additional amounts of those foods which are concentrated in energy value, as well as proteins, vitamins, and minerals Insofar as possible these additions to the diet should be made in accordance with the appetite and food preferences of the patient.

In calculating the number of calories per day the important principle is to be certain that the caloric value of the diet exceeds the total energy requirement per day in order to provide for storage of fat If possible the customary food intake should be investigated so that the new diet order can be based on the number of calories of the usual intake plus those necessary for the rate of weight increase which is desired. Caloric needs for normal individuals as estimated by the National Research Council are given in Table XI

Table XI. Caloric Needs for Normal Individuals

	Calories
Man (154 lbs or 70 Kg)	
Sedentary	2400
Physically active	3000
With heavy work	4500
Woman (123 lbs or 56 Kg)	
Sedentary	2000
Moderately active	2400
Very active	3000
Pregnancy (latter half)	2400
Lactation	3000
Children up to 12 years*	
Under 1 year	110/Kg
1 to 3 years	1200
4 to 6 years	1600
7 to 9 years	2000
10 to 12 years	2500
Children over 12 years*	
Girls 13 to 15 years	2600
16 to 20 years	2400
Boys 13 to 15 years	3200
16 to 20 years	3800

* Allowances for children are based on the needs for the middle year in each group (as 2, 5 8, etc) and are for moderate activity and for average weight at the middle year of the age group

If a weight gain of approximately two pounds a week is desired, an increase over the normal requirements of at least 1200 calories per day must be made. Naturally this gain will vary a great deal depending on the degree of activity of the patient, the water balance, and the nature of any accompanying disease

In any high calorie diet the foods chosen to increase calories should be selected with three factors in mind, listed here in order of importance:

1 Select those foods which will provide food constituents which are deficient in the patient's normal diet.

2. Choose those foods most acceptable to the patient.

3 Choose those foods which will have less "bulk" in the diet and provide highest energy value.

A sample high calorie (3500) diet would be as follows:

Foods for the Day	*Amount*
Eggs prepared any way	2
Meat, fish, or poultry, lean or medium fat	6 ounces
Bacon or sausage	1 ounce
Milk	1 quart
Cream (20 per cent)	½ cup
Butter, oleomargarine	4 tablespoons
Cereal	¾ cup
Bread, toast	6 slices
Potato or substitute	2 servings
Other vegetables	2 servings
Citrus fruit or juice	1 serving
Other fruit, stewed or canned	1 serving
Sugar, jelly, or honey	4 tablespoons
Desserts other than fruit	2 servings

Sample Meal Plan

Food	*Amount*
BREAKFAST	
Orange juice	1 4-ounce glass
Egg, fried	1
Bacon	4 slices
Toast, whole wheat	2 slices
Butter	1 tablespoon
Jelly	1 teaspoon
Sugar	2 teaspoons
Coffee	1 cup
Cream	2 tablespoons
MID-MORNING	
Oatmeal	¾ cup
Cream	¼ cup
Sugar	2 teaspoons
Milk	1 glass
LUNCHEON	
Roast veal	3 ounces
Steamed rice	½ cup
Carrot rings	½ cup
Roll	1 whole
Butter	1 tablespoon
Milk	1 glass
Tapioca pudding	1 serving

AFTERNOON

Eggnog	1 egg, 1 glass milk, 1 tablespoon sugar
Toast	1 slice
Butter	1 teaspoon
Jelly	1 teaspoon

DINNER

Meat patty	3 ounces
Baked potato	1
Green salad mixed	½ cup with 1 tablespoon dressing
Bread	1 slice
Butter	1 teaspoon
Apple pie	1 serving
Coffee	1 cup
Cream	2 tablespoons
Sugar	2 teaspoons

EVENING

Milk	1 glass, flavored as desired

Low Salt–High Calorie Diet

A low salt, high calorie diet would vary from the regular high calorie regimen in that the foods of high sodium content would be restricted. The following foods could be included in a sample 3200-calorie, low salt diet (approximately 3.0 Gm. of salt, depending on the salt content of the dessert allowed)

Foods for the Day

All foods prepared without added salt

Egg	1
Unsalted meat, fish, or poultry	3 ounces
Cream	½ cup
Milk	1½ cups
Unsalted bread	8 slices
Unsalted butter	4 tablespoons
Potato or rice	2 servings
Vegetables	2 servings (omit high sodium)
Fruit juice	3 8 ounce glasses
Sugar or jelly	4 tablespoons
Stewed or canned fruits	2 servings
Dessert other than fruit	1 serving

These foods would be divided into a meal plan in much the same manner as the regular high calorie diet given on the opposite page. It is often desirable and more palatable to divide such diets into smaller and more frequent meals as shown in that meal plan.

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